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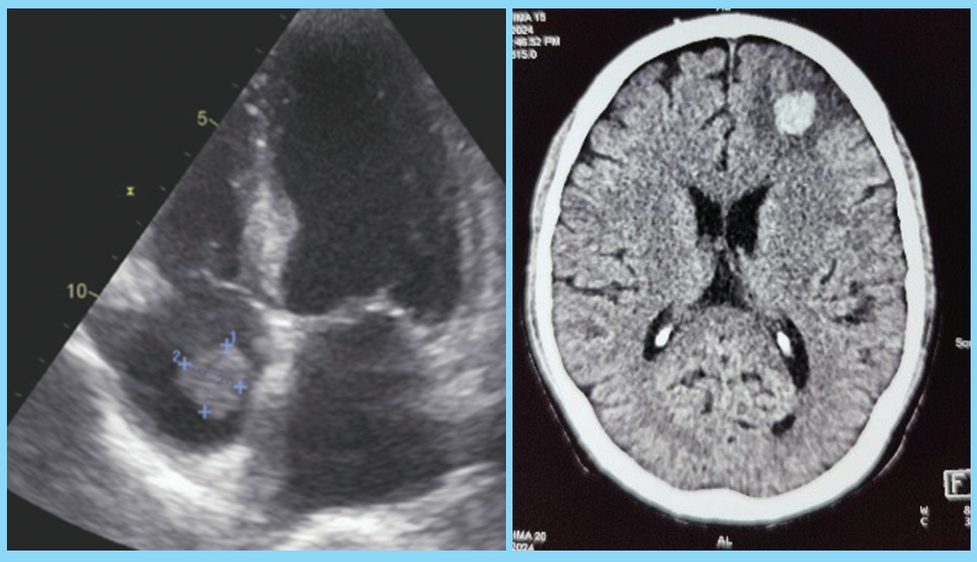

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ORIGINAL ARTICLE

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A Study of Clinical Assessment, Aetiology and Outcome of Patients Presenting with Altered Sensorium

Shivaputra Patil, RS Yadav**, Dharmendra Kumar Mekle***, Simmi Dube****, SV Subhash**

Abstract

Background: This study seeks to determine the clinical assessment methods, aetiology and clinical prognosis that are implemented among patients with altered sensorium in emergency.

Methodology: This research was designed as a prospective observational study on patients with altered sensorium (GCS <15) admitted in Department of Medicine, Hamidia Hospital over a period of 18 months. Detailed history was obtained and examination was done. Necessary investigations were done to determine the underlying cause and outcomes were assessed.

Results: This study was conducted on a total of 200 cases, where majority were males (68%) and 37.5% of the cases belonged to elderly age group. Most common presenting complaint was hemiparesis (29.5%). Most common aetiology was acute ischaemic stroke (21.5%) followed by infections (16%). There was 34.5% mortality rate. We observed a significant association of outcomes with age, presenting complaints and aetiology (p <0.05).

Conclusion: Altered sensorium is a significant medical condition with varied aetiologies and outcomes influenced by age, presenting complaints, and underlying morbidities. The study highlighted that age and specific presenting symptoms such as limb weakness and breathlessness are critical factors in patient outcomes. Haemorrhagic strokes and severe infections were associated with higher mortality, emphasizing the need for timely diagnosis and intervention.

Key words: Altered sensorium, infections, stroke.

Introduction

Altered sensorium encompasses a variety of clinical manifestations, including cognitive disorders, attention deficits, arousal abnormalities, and diminished levels of consciousness[1]. This condition presents a common challenge in emergency medicine, often with vague symptoms. Therefore, the task of diagnosing and managing patients with altered sensorium can be quite challenging for emergency physicians. Understanding how it develops and thoroughly evaluating the patient are crucial for improving the accuracy of diagnosis and effectiveness of treatment[2]. Clinical assessment plays a crucial role in evaluating patients with altered sensorium. It involves extensive neurological examination, cognitive assessment, and diagnostic investigations[3]. With a keen eye for detail and a methodical approach, clinicians are able to detect even the most subtle changes in consciousness, cognitive abilities, and neurological impairments. This allows for precise diagnoses and tailored treatments. In addition, the field of neuroimaging techniques and biochemical assays have made significant progress, allowing clinicians to better understand the underlying pathology with more accuracy and efficiency[4].

Understanding the causes of change in consciousness involves a wide range of complex factors, including neurological, systemic, and environmental influences. Neurological causes, such as traumatic brain injury, stroke, encephalitis, and seizures, play a significant role in many cases[5,6]. At the same time, there can be metabolic disturbances such as imbalances in electrolytes, hepatic encephalopathy, uraemic encephalopathy, and diabetic ketoacidosis that can cause changes in consciousness[7]. In addition, the diagnosis of infectious diseases such as bacterial meningitis and viral encephalitis can be quite challenging. It is important to approach the screening and treatment of these infections with great care.

Although altered sensorium is of great clinical importance, there is a lack of epidemiological studies on this topic globally. The outcome of patients with changes in mental state depends on how quickly and accurately they are diagnosed, and how promptly appropriate treatment is started. Swift recognition and intervention can help reduce the chances of complications, prevents any decline in neurological health, and improves the overall prognosis. This study seeks to determine the clinical assessment methods, aetiologies and clinical prognosis among the

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patients with altered sensorium.

Material and Methods

This research was designed as a prospective observational study on patients admitted to Medical Ward 1 and Medical Ward 2, Department of Medicine, Gandhi Medical College and associated Hamidia Hospital, Bhopal, Madhya Pradesh over a period of 18 months. All the patients presenting with Glasgow Coma Scale (GCS) score of less than 15, and new onset drowsiness or confusion of 1 week duration were included, whereas patients with chronic altered sensorium conditions (such as Alzheimer's disease, schizophrenia, and other psychiatric disorders), of age less than 13 years, and traumatic brain injury were excluded from the study.

The study was approved by the Institutional Ethics Committee (IEC) of Gandhi Medical College, Bhopal. Informed consents were obtained from all the participants or their legal health proxies (in case of minors or incapacitated patients). The confidentiality of patient data was strictly maintained throughout the study. Upon admission, the time and manner of admission along with detailed medical history were obtained. All the patients were subjected to detailed general and systemic examination. Laboratory tests were done which included complete blood counts, renal function tests with serum electrolytes, liver function tests (LFTs), and arterial blood gas (ABG) analysis and findings documented to determine the underlying cause. Apart from this, imaging studies such as ultrasound of abdomen and pelvis, computed tomography (CT) of the head, and magnetic resonance imaging (MRI) of the head were done. Electrocardiogram (ECG), electroencephalogram (EEG) and cerebrospinal fluid (CSF) analysis were done where indicated.

Aetiology of altered sensorium was established as:-

Primary Neurological: Cerebrovascular Accident (CVA), seizure disorder, meningoencephalitis.

Non-neurological: Metabolic, hepatic, renal, respiratory (RS), cardiovascular (CVS), sepsis with multiple organ dysfunction syndrome (MODS), pharmacologic/toxic.

Statistical Analysis

Data were analysed using IBM SPSS software version 20 (Statistical Package for Social Sciences, IBM Corp. Illinois Chicago). The Chi-square test was used to study the association between contributory factors and outcomes. A p value of <0.05 was considered statistically significant.

Results

This study was conducted on a total of 200 cases presenting with altered sensorium at our centre.

Table I: Distribution of patients according to baseline variables

Baseline variables		Number of patients (n = 200) (Per cent)
Gender	Female	64 (32.0)
	Male	136 (68.0)
Age (years)	13 - 20	4 ((2.0)
	21 - 30	30 (15.0)
	31 - 40	42 (21.0)
	41 - 50	24 (12.0)
	51 - 60	25 (12.5)
	>60	75 (37.5)
Complaints	Abnormal Body Movements	10 (5.0)
	Breathlessness	32 (16.0)
	Fever	32 (16.0)
	H/O Unknown Substance Ingestion	14 (7.0)
	Headache	3 (1.5)
	Jaundice	23 (11.5)
	Loss of Consciousness	5 (2.5)
	Pain Abdomen	13 (6.5)
	Vomiting	18 (9.0)
	Hemiparesis	59 (29.5)

68% of the patients with altered sensorium were males, and 37.5% of the cases belonged to elderly age group. Most common presenting complaint in the present study was hemiparesis (29.5%), followed by breathlessness (16%)

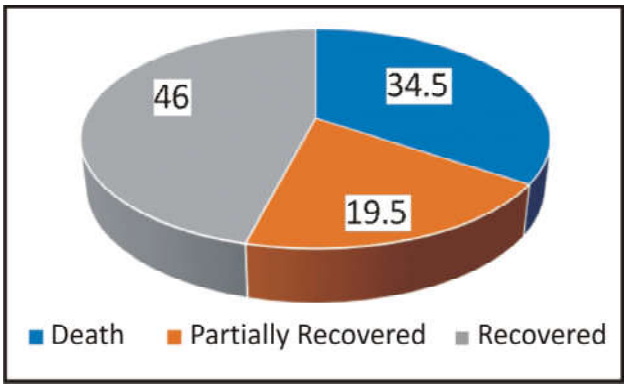

Fig. 1: *Distribution of patients according to outcome.*

and fever (16%) as shown in Table I.

Table II: Distribution as per aetiology

Aetiology	Number of patients	Per cent
CNS	**108**	**54.0**
Infections	32	16.0
Haemorrhagic stroke	20	10.0
Ischaemic stroke	43	21.5
ICSOL	3	1.5
Seizure disorder	10	5.0
Metabolic	**92**	**46.0**
Drugs/Toxin	14	7.0
Hyponatraemia	9	4.5
Hepatic	23	11.5
Hypoglycaemia	5	2.5
Ketosis	9	4.5
Respiratory	14	7.0
Uraemic encephalopathy	18	9.0

Primary CNS involvement was seen in 54% of the patients. Most common aetiology reported in the study was ischaemic stroke (21.5%), followed by infections (16%) and hepatic (11.5%). Other common aetiologies were uraemic encephalopathy (9%), drugs/toxin (7%) and respiratory (7%) (Table II).

Death was reported in 34.5% patients, 19.5% were partially recovered and 46% were fully recovered (Fig. 1).

Table III: Association of outcome with baseline variables and aetiology

Variables		Outcome			p value
		Death	Partially Recovered	Recovered	
Gender	Female	20	15	29	0.593
	Male	49	24	63	
Age (years)	13 - 20	1	1	2	0.001*
	21 - 30	7	0	23	
	31 - 40	12	3	27	
	41 - 50	8	4	12	
	51 - 60	9	3	13	
	>60	32	28	15	
Compl aints	Abnormal Body Movements	2	0	8	0.001*
	Breathlessness	6	0	8	
	Fever	10	1	21	
	H/O Unknown Substance Ingestion	5	0	9	
	Headache	1	2	0	
	Jaundice	8	0	15	
	Loss of Consciousness	2	0	3	
	Pain Abdomen	4	1	8	
	Vomiting	6	0	12	
	Hemiparesis	23	35	1	
Aetiology	Drugs/Toxin	5	0	9	0.001*
	Hyponatraemia	2	0	7	
	Haemorrhagic stroke	16	3	1	
	Hepatic	8	0	15	
	Hypoglycaemia	2	0	3	
	ICSOL	1	2	0	
	Infections	10	1	21	
	Ischaemic stroke	10	33	0	
	Ketosis	1	0	8	
	Respiratory	6	0	8	
	Seizure disorder	2	0	8	
	Uraemic encephalopathy	6	0	12	

Though we found no significant association of outcomes with gender ($p > 0.05$). Death was more common among the older patients (12/69), followed by those having age between 31 - 40 years (12/69) ($p < 0.05$). Death was more common in patients complaining of hemiparesis (n = 23/69) followed by breathlessness (n = 10/69) and jaundice (n = 8/69) ($p < 0.05$). Also, death was more among the patients with haemorrhagic stroke (n = 16/69) followed by infective causes (n = 10/69) and ischaemic stroke (n = 10/69) ($p < 0.05$) (Table III).

Discussions

In our study, the majority of patients presenting with altered sensorium were over 60 years of age (37.5%) and were males. Our study found a wider age range, with a notable number of patients over the age of 60 years. In the study conducted by Rai *et al*[9], it was observed that a significant number of patients were males (68%) with an average age of 45.53 ± 20 years. This could be attributed to variations in study settings and populations, as well as the specific emphasis on EEG predictors in Rai's study, which may have attracted a distinct patient demography.

In a study conducted by Raghu *et al*[10], it was discovered that the largest portion of patients fell within the 31 - 40 years age group. Males accounted for 31% of the patients, while females made up 22%. In our study, we observed that older age groups were more affected by altered

sensorium, which may be attributed to various geographical and environmental factors influencing its aetiology in different regions. This finding is in contrast to the younger age range observed in other studies. According to Jali *et al*[2], the study found that the majority of patients with altered sensorium were aged 60 years and above (32%). This aligns with our own findings and indicates that age-related factors, such as co-morbidities and higher susceptibility to neurological conditions, are important contributors to the presentation of altered sensorium in older populations. In the study conducted by Namindla *et al*[1], the age group most frequently affected was 51 - 60 years (28%), followed by 41 - 50 years (21%) and 61 - 70 years (18%), with an average age of 49.12 ± 14.77 years. This distribution indicated a pattern favouring middle to older age groups, which aligns with our observation that a considerable number of patients are over 60 years old. The slight differences in age distribution across these studies could be attributed to variations in healthcare access and the specific health conditions that are more common in the study populations. Our study and other similar studies have found that older adults are more likely to experience altered sensorium. This is likely due to the fact that older individuals often have multiple comorbidities, such as cardiovascular diseases, diabetes, and neurodegenerative disorders, which can contribute to altered sensorium[11,12]. In addition, there are certain physiological changes that occur with age, such as reduced blood flow to the brain and increased vulnerability to metabolic disruptions, which may also contribute to the situation.

Among patients with altered sensorium, hemiparesis was the most common presenting complaint (29.5%). This was followed by breathlessness (16%), fever (16%), jaundice (11.5%), vomiting (9%), history of unknown substance ingestion (7%), and abdominal pain (6.5%). These findings are consistent with the study conducted by Raghu *et al*[10], which found that fever (36%), headache (56%), vomiting (53%), and weakness (14%) were common symptoms in patients with altered sensorium. Their study also observed that infective causes were the most prevalent, followed by cerebrovascular accidents (CVAs), metabolic, and other causes. These findings indicate that these symptoms are common indicators of altered sensorium in various patient populations.

Kanich *et al*[13] found that among emergency department patients with altered mental status (AMS), the most common causes were neurological (28%) and toxicological (21%), followed by trauma (14%), psychiatric (14%), and infectious causes (10%). Diagnosing AMS can be quite complex due to the wide range of causes and symptoms, including lethargy and unusual behavior. Tuma *et al*[14] emphasized the complex factors contributing to AMS in cancer patients, included medications, metabolic issues, and infections. This complexity is reflected in our study, where symptoms such as weakness and vomiting suggest various possible underlying causes, requiring a thorough diagnostic approach.

Mahmood *et al*[15] discovered that the most prevalent causes of AMS were pyogenic meningitis, encephalitis, and cerebral malaria. It was also noted that fever was a persistent symptom in these cases. Our findings indicate that fever was a common complaint, highlighting the need to consider infectious causes in patients who have changes in their mental state. The occurrence of vomiting and abdominal pain in our study aligns with the results of Arora *et al*[16], who observed gastrointestinal symptoms in pediatric patients experiencing hyperosmolar diabetic ketoacidosis and hyperglycaemic hyperosmolar state, resulting in changes in mental alertness.

We found that a significant portion of patients with altered sensorium did not survive, while others experienced varying degrees of recovery. The high mortality rate underscores the serious nature of changes in consciousness. In the study conducted by Raghu *et al*[10], high mortality rates were observed in severe cases such as intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH). On the other hand, patients with metabolic causes like hypoglycaemia and Wernicke's encephalopathy showed better recovery rates. The correlation between these findings highlights the significance of pre-existing conditions on the outcomes of patients. Mahmood *et al*[15] also found significant mortality caused by infections such as pyogenic meningitis and encephalitis. This observation further supports our findings that infections play a significant role in increasine mortality rates.

In a study by Kanich *et al*[13], the causes of AMS in emergency departments were found to be primarily neurologic and toxicologic, resulting in a relatively low mortality rate of 9%. Nevertheless, their research highlighted the significance of patient history and physical examination in diagnosing AMS, underscoring its critical role in determining the prognosis and guiding treatment. These findings indicate that infections and severe neurological conditions play a significant role in higher mortality rates. It is crucial to diagnose and intervene promptly and comprehensively to improve recovery outcomes in patients with altered sensorium.

Our study found that 54% of patients with altered sensorium had involvement of the central nervous system (CNS), while metabolic causes were responsible for the remaining 46%. These findings align with findings of multiple other studies. Jali *et al*[2] found that altered

sensorium was primarily caused by cerebrovascular accidents (CVAs), accounting for 38% of cases. Metabolic causes and infections followed closely behind, making up 28% and 24% of cases, respectively. Raghu *et al*[10] found a high prevalence of CNS involvement. Their study showed that neurological causes, especially CVAs, were major factors contributing to changes in sensorium, with metabolic causes also playing a significant role. Kanich *et al*[13] discovered that neurologic causes were the primary reason for altered mental status (AMS) in emergency department patients, accounting for 28% of cases. They also noted the significance of metabolic causes in contributing to AMS.

Our study found that ischaemic stroke was the most common cause of altered sensorium, accounting for 21.5% of cases. Infective causes were the second most common, at 16%, followed by hepatic causes at 11.5%. This high prevalence of CNS involvement aligns with the findings of Raghu *et al*[10].

Manji *et al*[17] emphasized the significance of metabolic encephalopathy, specifically hyponatraemia, as a common cause of AMS in elderly patients. Similarly, Mahmood *et al*[15] found that metabolic disorders such as diabetic ketoacidosis and hepatic encephalopathy frequently contribute to altered sensorium. The consistency observed in these studies emphasizes the significant contributions of both central nervous system and metabolic factors in the development of changes in consciousness. Understanding and addressing these underlying conditions is crucial for enhancing patient outcomes. These studies highlight the significance of thorough diagnostic evaluations in effectively identifying and treating the various causes of changes in consciousness.

Our study found that ischaemic stroke was the most common cause of altered sensorium, accounting for 21.5% of cases. Infective causes followed closelybehind at 16%, while hepatic causes accounted for 11.5%. In addition, patients with haemorrhagic stroke had a higher mortality rate (16/69), followed by infective causes (10/69) and ischaemic stroke (10/69).

According to Jali *et al*[2], patients with cerebrovascular accidents (CVAs), especially those with intracerebral haemorrhage (ICH), had alarmingly high mortality rates, with a 100% fatality rate in their study. Infections and metabolic causes were found to have different outcomes, with metabolic causes generally resulting in better recovery rates.

Manji *et al*[17] shed light on the high mortality rates observed among patients with severe neurological and infectious conditions. Kanich *et al*[13] also highlighted thesignificance of timely intervention in improving outcomes, particularly in cases involving neurologic and infectious causes. Mahmood *et al*[15] discovered that infectious causes such as pyogenic meningitis and encephalitis were common and had high mortality rates. Raghu *et al*[10] found that SAH patients with altered sensorium at presentation had a 100% mortality rate. Our findings align with those of other studies, highlighting the significance of comprehending the diverse causes and their effects on patient outcomes in cases of altered sensorium.

Our study revealed strong correlations between age distribution and outcomes, with higher mortality rate in older patients. Patients experiencing hemiparesis (23/69), breathlessness (10/69), and jaundice (8/69) had a higher incidence of death. According to Jali *et al*[2], it was observed that the mortality rates were higher in older age groups, especially in individuals over 60 years of age. Their study highlighted the importance of age in determining outcomes, as older patients often have multiple co-morbidities that can lead to more unfavorable prognoses. Raghu *et al*[10] discovered that older patients with changes in their mental state experienced worse outcomes as compared to younger patients. Mahmood *et al*[15] found that older patients with fever and altered sensorium had a higher mortality rate. This was especially true for those who had underlying infections and co-morbidities.

Our study highlights the crucial role of early and accurate diagnosis, especially in older patients and those with severe symptoms. The correlation between age distribution and outcomes, as well as the significant impact of presenting complaints, further emphasizes this importance. These findings are consistent with previous research, highlighting the importance of conducting thorough evaluation and implementing specific treatments to enhance patient outcomes in situations involving changes in mental status.

The limitations of our study include the observational design, which may introduce bias and limit the ability to establish causality. The study is conducted at a single centre, potentially affecting the generalizability of the findings to other populations and settings. The exclusion of patients with chronic altered sensorium and traumatic brain injuries might limit the comprehensiveness of the study. Additionally, the reliance on self-reported medical histories and the accuracy of clinical assessments could be subject to variability. The sample size, while substantial, may still not capture all potential variations in aetiologies and outcomes, and the study's duration may not be sufficient to observe long-term outcomes and trends.

Conclusion

We found that altered sensorium is a significant medical condition with varied aetiologies and outcomes influenced by age, presenting complaints, and underlying causes. The

majority of patients were older than 60 years of age, and common aetiologies included ischemic stroke, infections, and hepatic failure. The study highlights that age and specific presenting symptoms such as limb weakness and breathlessness are critical factors in patient outcomes. Hemorrhagic strokes and severe infections were associated with higher mortality, emphasizing the need for timely and accurate diagnosis and intervention. Despite no significant differences in the outcomes based on gender, understanding the varied aetiologies and their impact is crucial for improving patient prognosis through comprehensive assessment and targeted treatment strategies. These findings align with existing literature, underscoring the importance of addressing the underlying causes to enhance recovery rates and reduce mortality in patients with altered sensorium.

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ORIGINAL ARTICLE

JIACM 2025; 26 (3): 92-96

Assessment of Sarcopenia with 30 and 90 Days Morbidity and Mortality Outcomes in Child-Turcotte-Pugh (CTP) B and C Cirrhosis

Karuna Anot, Pritam Singh**, Atul Sachdev***, Swati Garg*, Sarabmeet Singh Lehl**, Ravinder Kaur*****

Abstract

Background: Sarcopenia is defined as progressive loss of skeletal mass, strength and physical performance. Our study focused on evaluation of sarcopenia as an independent factor to predict with 30 and 90 days morbidity and mortality outcomes in CTP B and C cirrhosis.

Methods: Sarcopenia was assessed by muscle mass, strength and physical performance and each parameter was individually scored.

Results: 50 patients with confirmed cirrhosis CTP B and C were included and assessed for sarcopenia. 27(54%) patients were CTP grade B and 23 (46%) were CTP grade C with a mean age of 45.26 ± 12.731 years. Sarcopenia was present in 36 (72%) patients; 12 (24%) had moderate and 24 (48%) had severe sarcopenia. CTP C group (63%) had more significant sarcopenia than CTP B group (82.6%) (p = 0.01). Significant morbidity at 30 (p = 0.03) and 90 days (p = 0.01) was seen. The association of 30 and 90 days mortality is also significant (p <0.01).

Conclusion: Sarcopenia can be considered as a good indicator of morbidity and mortality in the patients of cirrhosis and has a high concordance with the CTP score.

Key words: Sarcopenia; Child-Turcotte-Pugh (CTP); cirrhosis; morbidity; mortality.

Abbreviations: CTP: Child-Turcotte-Pugh; BIA: Bioimpendance analysis; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; SPPB: Short Physical Performance Battery; MELD: Model for end-stage liver diseases; MDCT: Multi-Detector Computed Tomography; PI: Psoas Index; RPA: Right Psoas Area; LPA: Left Psoas Area; HU: Hounsfield Unit; HUAC: Hounsfield Unit Average Calculation; PTMT/H: Psoas Muscle Thickness for Height; CLDQ: Chronic Liver Disease Questionnaire; HE: Hepatic encephalopathy; UGIB: Upper gastrointestinal bleed; HRS: Hepato-renal syndrome; TPMT: Transverse psoas muscle thickness; SMI: Skeletal muscle index; BCCA: Branched-chain amino acid.

Introduction

Sarcopenia as a term was devised by Irwin Rosenberg in 1989 and derived from two Greek words-'Sarx' which means flesh and 'Penia' which means loss[1]. It is defined as progressive loss of skeletal mass, strength and physical performance[2-4]. It is categorised as primary and secondary[4]. Primary sarcopenia is age related while secondary sarcopenia is due to disease, nutrition and decreased activity. Muscle mass can be calculated by radiological and conventionally accepted methods including bioimpendance analysis (BIA) and anthropometry. Radiological methods like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) have the advantage of direct visualisation and measurements of tissue compartments and are not affected by fluid accumulation (ascites) as well as simultaneous evaluation of the liver is done[5]. Muscle strength is assessed with hand grip, knee flexion/extension, peak expiratory flow. Physical performance is assessed by usual gait speed, timed get-up-and-go test, stair climb power test and Short Physical Performance Battery (SPPB)[6].

Cirrhosis is a hypercatabolic state and is associated with sarcopenia and malnutrition[7,8]. The possible reasons cited for hypercatabolic state are hyperdynamic circulation, systemic inflammation and subclinical endotoxaemia related to intestinal bacterial translocation. Sarcopenia in cirrhosis is due to inadequate dietary intake, metabolic disturbances, hypercatabolism and associated clinical or subclinical malabsorption.

Sarcopenia and poor nutrition is associated with adverse outcomes in cirrhosis[7-13]. The prevalence of sarcopenia in cirrhotics is reported to be between 40 - 68%[10,12]. It is an independent risk factor for mortality in patients with cirrhosis[9-13]. However, traditional scores like modified Child-

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Turcotte-Pugh (CTP) or the model for end-stage liver diseases (MELD) do not include sarcopenia as a criterion for prognosis. Various other tools have been used over time for the assessment of the nutritional status in patients with cirrhosis but there has been a lack of reproducibility, objectivity, and prognostic performance which limits their wider application[7].

Hence, sarcopenia quantified by an objective method along with other commonly used prognostic tools has the potential to improve prognostication in patients with cirrhosis. There is paucity of data on sarcopenia and its correlation with cirrhosis in India. Our study focused on evaluation of sarcopenia as an independent factor to predict with 30 and 90 days morbidity and mortality outcomes in CTP B and C cirrhosis.

Material and Methods

This study was conducted in a tertiary care facility at Government Medical College and Hospital, Chandigarh, India. All patients over 18 years of age diagnosed with cirrhosis due to various aetiologies belonging to CTP class B and C were included. CTP A cirrhotics and patients having associated malignancy were excluded. Cirrhosis was confirmed by clinical and radiological methods. Sarcopenia was assessed by muscle mass, strength and physical performance and each parameter was individually scored (as indicated in Table I)[4]. The tests were done by one blinded investigator to avoid bias.

Table I: Parameters to assess sarcopenia.

S.No.	Parameter	Methods	Points
1.	Muscle mass	CT scan abdomen done at two levels; one at L3 vertebral level and the other at umbilical level[14].	1
2.	Muscle strength	Done with hand held Jamar dynamometer[15].	1
3.	Physical performance	Done with Short Physical Performance Battery (SPPB).[6]	1

For muscle mass, CT scan of abdomen on 64 slice Multi-Detector Computed Tomography (MDCT) scanner (Inbuilt software) was done at two levels; two axial images were taken; one at L3 vertebral level and the other at umbilical level to look for psoas muscle parameter[14]. One point was given to reduced muscle mass, if all the 3 criteria of CT abdomen were fulfilled as given below:

1. At L3 vertebral level, Psoas Index (PI) was measured normalising by the square of the height.

   PI = [Right Psoas Area (RPA) + Left Psoas Area (LPA)]/ height^2 in cm^2/m^2

   PI $\leq$7.77 cm^2/m^2 in males and $\leq$4.75 cm^2/m^2 in females was significant and indicated reduced muscle mass[14].

2. At L3, Hounsfield Unit Average Calculation (HUAC) was done after taking mean of three values on each side[14].

   HUAC = [(Right mean psoas HU density x RPA) + (Left mean psoas HU density x LPA)]/(Total Psoas Area).

   HUAC $\leq$38.5 Hounsfield unit was significant indicating reduced muscle mass[14].

3. At umbilical level, Psoas Muscle Thickness for Height (PMTH/H) was done after normalising the patient's height[10].

   PMTH/H <16.8 mm was taken as significant indicating reduced muscle mass[10].

Muscle strength was assessed with hand held Jamar dynamometer. An average of three values was taken. A cut-off value of $\leq$30 Kg in males and $\leq$20 Kg in females was considered significant for reduced muscle strength and one point was given[15].

Physical performance was assessed using the Short Physical Performance Battery (SPPB) which is a battery of tests used to check mobility and physical performance. A final score of $\leq$8 indicates reduced physical performance and one point was given if the score was met[6].

Then patients were stratified into various categories namely pre-sarcopenia, moderate sarcopenia, and severe sarcopenia; although literature categorises moderate sarcopenia as sarcopenia[4] (Table II).

Table II: Criteria based categorisation of Sarcopenia[4].

Groups	Categorisation of sarcopenia	Criteria	Points
Non-Sarcopenia group	No Sarcopenia	No criteria fulfilled	0 out of 3
	Pre-Sarcopenia	Reduced muscle mass only	1 out of 3
Sarcopenia group	Moderate Sarcopenia	Reduced muscle mass + Reduced muscle strength/ reduced physical performance	2 out of 3
	Severe Sarcopenia	Reduced muscle mass + Reduced muscle strength + Reduced physical performance	3 out of 3

Patients meeting minimum 2 out of 3 criteria are defined as sarcopenic. These are subcategorised into moderate (if 2/3 criteria fulfilled) and severe (if 3/3 criteria fulfilled). Pre-sarcopenia was defined if 1/3 criteria met. So there were two groups- Non-Sarcopenia group and Sarcopenia group (Table II).

The patients followed up after discharge at day 30 and 90 and the data was analysed for association with sarcopenia. Morbidity was assessed by using Chronic Liver Disease Questionnaire (CLDQ), a validated score used to assess

quality-of-life and consists of 29 items on a seven-point Likert scale, with higher scores indicating a better quality-of-life. Out of a total of 7, a cut-off at <3.5 was considered as significant. Mortality was recorded along with the immediate cause of death.

Results

Baseline demographic and clinical characteristics of 50 patients included in the study are presented in Table III; 39 (78%) patients were males and 11 (22%) females. The mean age of the patients was 45.26 ± 12.731 years (Range 19 - 76 years). 27 (54%) patients were CTP grade B and 23 (46%) were CTP grade C. Various aetiologies identified were alcohol in 26 (52%), hepatitis B in 8 (16%), hepatitis C in 7 (14%), NASH in 4 (8%) and cryptogenic in 5 (10%) patients. Co-morbid illnesses like diabetes mellitus present in 4 (8%) and hypertension in 6 (12%) were also recorded and these patients belonged to sarcopenia group. There were no other co-morbidities.

Table III: Baseline characteristics of study population

Characteristics	n (%)
Age	45.26 ± 12.731 (Range 19 - 76 years)
Males	39 (78%)
Females	11 (22%)
Aetiologies	
– Alcohol	26 (52%)
– Hepatitis B	8 (16%)
– Hepatitis C	7 (14%)
– NASH	4 (8%)
– Cryptogenic	5 (10%)
Co-morbidity	
– Diabetes mellitus	4 (8%)
– Hypertension	6 (12%)
– None	40 (80%)
CTP	
– CTP B	27 (54%)
– CTP C	23 (46%)
Sarcopenia	36 (72%)
Categorisation of Sarcopenia	
– No Sarcopenia	5 (10%)
– Pre-Sarcopenia	9 (18%)
– Moderate Sarcopenia	12 (24%)
– Severe Sarcopenia	24 (48%)
Total Morbidity	
– 30 day	22/35 (62.85%)
– 90 day	15/26 (57.69%)
Total Mortality	
– 30 day	15 (30%)
– 90 day	24 (48%)

Sarcopenia was present in 36 (72%) patients; 12 (24%) had moderate and 24 (48%) had severe sarcopenia. Both moderate and severe sarcopenia together constituted the sarcopenia group while no sarcopenia and pre-sarcopenia were in non-sarcopenia group (Table III). Sarcopenia was present in 6 (54.5%) females and 30 (76.9%) males but the correlation with gender was statistically insignificant (p = 0.15). CTP C group had more significant sarcopenia than CTP B group, i.e., 17 (63%) out of 27 patients of CTP B and 19 (82.6%) out of 23 patients of CTP C had sarcopenia (p = 0.01).

Significant morbidity at 30 days was seen in 22 patients - 16 belonged to sarcopenia group and 6 to pre-sarcopenia group (p = 0.03). Significant morbidity at 90 days was seen in 15 patients - 10 belonged to sarcopenia group and 5 to pre-sarcopenia group (p = 0.01). No morbidity was seen in no sarcopenia group at both 30 and 90 days (Table IV).

At 30 days 15 (30%) patients died - all belonging to sarcopenia group (p <0.01), and at 90 days 24 (48%) patients died - 22 belonging to sarcopenia group and 2 to pre-sarcopenia group (p <0.01). (cause of mortality as mentioned in Table IV).

Morbidity and mortality were then compared with moderate and severe sarcopenia. In moderate sarcopenia group, 3 patients died at 30 days (p = 0.06) and 5 patients at 90 days (p = 0.01) (Table V). Significant morbidity at 30 days was seen in 7 patients (p = 0.26) while at 90 days 5 patients had significant morbidity (p = 0.32).

In severe sarcopenia group, 12 patients died at 30 days (p = 0.002) and 17 patients died at 90 days (p = 0.001). Significant morbidity at 30 days was seen in 9 patients (p = 0.38) and at 90 days 5 patients had significant morbidity (p = 0.18).

Other parameters assessed like ascites, which was present in 45 (90%) patients (p = 0.05). Out of which, 9 (18%) had mild, 17 (35%) had moderate and 19 (38%) had gross ascites. Hepatic encephalopathy (HE) was present in 20 (40%) patients (p = 0.42). 8 (16%) had grade I HE, 7 (14%) had grade II HE, 3 (6%) had grade III and only 2 (4%) had grade IV HE. Patients with sarcopenia had lower mean albumin level of 2.5, as compared to non-sarcopenia group with 2.9 (p = 0.01). Mean serum bilirubin in non-sarcopenia group was 3.4, while in sarcopenia group it was 6.0 (p = 0.29). Mean INR in patients with sarcopenia was 1.72 while in non-sarcopenia group it was 1.49 (p = 0.15).

Table IV: Characteristics of sarcopenia and non-sarcopenia group

Characteristics	Non-Sarcopenia Group (no and pre-sarcopenia)	Sarcopenia Group (moderate + severe sarcopenia)	p value
Gender			0.15
– Males	9	30	
– Females	5	6	
CTP (Average = 9.74 ± 2.02)			0.01
– B	10	17	
– C	4	19	
Aetiologies			
– Alcohol	6	20	<0.01
– Hepatitis B	4	4	0.20
– Hepatitis C	3	4	0.20
– NASH	0	4	0.20
– Cryptogenic	1	4	0.20
Morbidity			
– At 30 day	6	16	0.03
– At 90 day	5	10	0.01
Mortality			
– 30 day	0	15	<0.01
– 90 day	2	22	<0.01
Cause of Mortality			
– At 30 day			
UGIBHE	0	5	0.14
Sepsis	0	1	053
Shock	0	3	0.27
HRS	0	1	0.53
Others	0	0	1.5
– At 90 day			
UGIB	0	8	0.05
HE	1	7	0.10
Sepsis	0	2	0.37
Shock	1	3	0.27
HRS	0	1	0.53
Others	0	1	0.53

**CTP: Child-Turcotte-Pugh Score, UGIB: upper gastrointestinal bleed, HE: hepatic encephalopathy, HRS: hepato-renal syndrome.*

Table v: Categorisation of sarcopenia and correlation with morbidity and mortality - 30 and 90 days

	Total patients	30 day Morbidity	P value	90 day Morbidity	P value	30 day Mortality	P value	90 day Mortality	P value
No Sarcopenia	5	0	0.02	0	0.02	0	0.02	0	0.02
Pre-sarcopenia	9	5	0.34	5	0.34	0	0.03	2	0.09
Moderate Sarcopenia	12	7	0.26	5	0.32	3	0.06	5	0.01
Severe Sarcopenia	24	9	0.38	5	0.18	12	0.002	17	0.001

Discussion

Sarcopenia has been observed to be an emerging prognostic factor in determining mortality in patients with cirrhosis[9-13]. We assessed sarcopenia in CTP B and C cirrhotic patients and it's correlation with 30 and 90 days morbidity and

mortality. We found a prevalence of sarcopenia in 72% patients (36/50), which is higher than the data available in existing literature (40 - 68%)[10,12]. We excluded CTP A patients who are relatively less sick, while the other studies did not exclude them.

In a study conducted by Montano loza *et al* sarcopenia was observed in 40% patients (45/112)[12]. Hanai *et al* observed sarcopenia in 68% patients (89/130)[10]. Various methods for studying muscle mass have been used in different studies namely PMTH/H, PI, HUAC, TPMT (transverse psoas muscle thickness), SMI (skeletal muscle index). There is no study which has compared these parameters with each other. However, all these parameters do indicate the muscle mass and measurements have been defined for each parameter indicating sarcopenia. Montano lazo *et al* and Hanai *et al* calculated sarcopenia using SMI at L3 level while we estimated psoas muscle at two levels; PMTH/H at umbilical level and PI and HUAC at L3 level. Durand *et al* calculated TPMT at the level of umbilicus[9]. Though the study did not calculate sarcopenia like our study but there was a 15% increase in mortality risk per unit decrease in TPMT/height and it was significantly associated with mortality, independent of the MELD and MELD-Na scores[9].

In our study sarcopenia has been categorised into pre-sarcopenia, moderate sarcopenia and severe sarcopenia. We did not come across any study categorising sarcopenia; hence the results cannot be compared. The patients were followed up for morbidity with CLDQ questionnaire at 30 and 90 days and higher morbidity was seen in sarcopenic patients at both 30 and 90 days. The correlation of sarcopenia in cirrhosis has not been studied though CLDQ questionnaire for assessing the morbidity in past and we have done it for first time and hence the results cannot be compared. Janani *et al* observed health related quality-of-life in cirrhosis patients using CLDQ questionnaire and did not correlate it with sarcopenia[17]. There were 149 patients (44-CTP A, 49-CTP B and 56-CTP C) studied, out of which CTP C cirrhotics had significantly higher complications as compared to CTP A and B indicating poor quality-of-life.

The association of at 30 and 90 days mortality in patients with CTP B and C cirrhosis with sarcopenia is significant ($p < 0.01$). Patients with severe sarcopenia had higher mortality as compared to pre and no sarcopenia. Montano Loza *et al* also observed shorter median survival time in patients with sarcopenia, i.e., 19 ± 6 months compared with 34 ± 11 months among non-sarcopenia patients ($p = 0.005$)[12]. Hanai *et al* also identified significantly higher mortality in sarcopenic patients ($p = 0.01$)[10]. Hanai *et al* also determined the outcomes of branched-chain amino acid (BCCA) supplementation and it improved the survival in sarcopenic patients ($p < 0.01$)[10]. Our study was an observational study and no intervention in form of nutritional supplements was studied.

Hence, sarcopenia can be considered as a good indicator of morbidity and mortality in the patients of cirrhosis and has a high concordance with the CTP score. Therefore, quantification of sarcopenia by an objective method along with commonly used prognostic systems may improve prognostication in patients with cirrhosis and larger studies are needed to evaluate these aspects.

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ORIGINAL ARTICLE

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A Retrospective Study of Outcomes of Acute Kidney Injury In the Medical Intensive Care Unit

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Abstract

***Background:** Acute Kidney Injury (AKI) is a serious complication in ICU patients, linked to high morbidity and mortality. Common causes include systemic illnesses, sepsis, hypotension, and nephrotoxic interventions. Early detection and management are critical for better outcomes. This study examines AKI incidence, risk factors, and outcomes in South Gujarat, emphasizing co-morbidities, causes, and the impact of interventions like dialysis.*

***Methods:** A retrospective observational study was conducted on 100 patients admitted to the ICU of a tertiary care hospital from July 2022 to September 2023. All patients were diagnosed with AKI based on the KDIGO criteria. Data on demographics, co-morbidities, aetiologies, and outcomes were collected using pre-formed case record forms. Statistical analysis was performed using IBM SPSS software to evaluate the influence of various factors on patient outcomes.*

***Results:** Sepsis was the leading cause of AKI, and infections such as malaria contributed significantly, with a mortality rate of 62.5% for malaria-related AKI. The most common co-morbidities were hypertension and diabetes mellitus. Patients receiving dialysis had significantly better recovery rates (97.3%) compared to those who did not receive dialysis (68%). Overall, 64% of patients recovered, 12% progressed to chronic kidney disease (CKD), and 24% succumbed to the condition.*

***Conclusions:** This study underscores the high incidence of AKI in ICU settings, with infections as the primary aetiology. Timely dialysis and effective management of underlying conditions significantly enhance the patient outcomes.*

***Key words:** Acute Kidney Injury, Intensive Care Unit, sepsis, dialysis.*

Introduction

Acute Kidney Injury (AKI) is a commonly prevalent complication in critically ill patients admitted to the intensive care units (ICUs). Defined by an abrupt loss of kidney function, AKI adversely impacts the clinical outcomes, increasing morbidity, mortality, and healthcare costs. Global data suggests that AKI affects up to 50% of ICU patients, with variation in incidence depending upon the patient population and healthcare setting[1]. Despite advancements in intensive care medicine, AKI remains a formidable challenge due to its multifactorial aetiology, encompassing conditions like sepsis, hypovolaemia, and nephrotoxic exposure.

In the ICU, AKI is often an interplay of systemic illnesses and treatment-related factors. Conditions such as sepsis and hypotension contribute to a hypo perfused state, while therapeutic interventions, including vasoactive drugs and mechanical ventilation, may further exacerbate renal stress[2]. The dynamic environment of the ICU makes it imperative to recognise and address these factors promptly to mitigate AKI progression. Studies indicate that early identification and targeted interventions are pivotal in improving patient outcomes, reducing the risk of transitioning to chronic kidney disease (CKD), and decreasing mortality rates[3].

The burden of AKI is not uniformly distributed but varies by demographic, geographic, and institutional characteristics. South Gujarat, as a region with diverse socio-economic and health determinants, provides a unique context for studying AKI. Limited data are available from this region regarding the demographic profiles, co-morbidities, and risk factors of ICU patients developing AKI. Understanding these aspects can guide the development of region-specific management protocols, improving outcomes for this vulnerable population.

Co-morbidities like diabetes mellitus, hypertension, and cardiovascular diseases are well-established risk factors for AKI. These conditions predispose individuals to haemodynamic instability, endothelial dysfunction, and increased susceptibility to nephrotoxic insults. Furthermore, the prevalence of AKI is higher among elderly patients, likely due to age-related decline in renal reserve and higher burden of comorbidities[4]. Identifying such high-risk groups is essential for devising preventive strategies, including optimizing fluid management and avoiding unnecessary

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nephrotoxic interventions.

Outcomes of AKI in the ICU are multifaceted, ranging from complete recovery of renal function to progression to CKD or end-stage renal disease (ESRD). Mortality rates among ICU patients with AKI remain alarmingly high, with estimates ranging between 30 - 50% depending on severity and underlying aetiology. Recovery trajectories are influenced by several factors, including the timeliness of AKI recognition, severity at onset, and adequacy of supportive care. Renal replacement therapy (RRT) is often employed in severe cases; however, its use carries inherent risks and resource implications. Emerging evidence underscores the importance of individualised decision-making regarding RRT initiation to balance benefits against potential harms[5].

Another critical area of exploration is the identification of modifiable variables that can improve AKI outcomes. Strategies such as early goal-directed therapy, judicious use of potential nephrotoxic agents, and implementation of AKI care bundles have shown promise in reducing incidence and improving recovery rates. Moreover, advancements in biomarkers for early AKI detection, including neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1), hold potential for transforming the diagnostic landscape, enabling preemptive intervention[6].

The present study seeks to address these gaps in knowledge by providing a comprehensive evaluation of AKI outcomes in a tertiary care medical ICU in South Gujarat. Specifically, aiming to analyse the incidence, prevalence, and demographic characteristics of AKI, identify associated risk factors and co-morbidities, and assess short- and long-term patient outcomes. The findings will contribute valuable insights for optimising AKI management and informing clinical decision-making in similar settings.

By focusing on a geographically distinct population, this study adds to the growing body of evidence on AKI, bridging the gap between global research and local healthcare practices. The results are anticipated to drive quality improvement initiatives, ultimately enhancing the care of critically ill patients in the ICUs.

Material and Methods

Study Setting

This study was conducted in the Medical ICU of a tertiary care hospital in South Gujarat, India.

Study Design

A retrospective observational study.

Study Subjects

All patients diagnosed with AKI and admitted to the Medical ICU during the study period.

Inclusion Criteria

- Patients >18 years with decreased urine output.
- AKI diagnosis based on KDIGO criteria:
  - Serum creatinine increases ≥0.3 mg/dL within 48 hours or ≥1.5 times baseline within 7 days.
  - Urine output <0.5 mL/kg/h for 6 hours.
- Baseline serum creatinine of 1.3 mg/dL considered normal.

Exclusion Criteria

- Age <18 or >90 years.
- Pregnant women.
- Chronic kidney disease (CKD) patients.

Sample Size

Using hypothesis testing, the required sample size was 80, based on a 30% prevalence and 10% margin of error. Data from 100 patients was analysed.

Study Period

Data was collected from July 2022 to September 2023 (15 months), with 5 additional months for analysis.

Sampling Technique

Purposive sampling was employed.

Study Tools

Data was recorded using a pre-formed case record form (CRF).

Data Collection

Following Institutional Ethics Committee (IEC) approval, demographic and clinical data were collected, including age, sex, symptoms, co-morbidities, and outcomes.

Investigations

Complete blood counts, renal function tests, serum electrolytes, calcium, phosphate, urine analysis, bicarbonate, eGFR, creatinine clearance, and abdominal ultrasound were included during initial investigations.

Outcome Measures

1. **Recovery:** Kidney function restored to baseline.

2. **Progression to CKD:** Persistent dysfunction post-AKI.
3. **Death:** AKI-related mortality.

Statistical Analysis

Data were entered into Microsoft Excel and analysed by appropriate statistical tests using IBM SPSS.

Results

The study enrolled 100 participants, out of which 60 were male and 40 were female.

Fig. 1 shows the age distribution of the study participants, with the majority being in the younger age groups. The highest percentage (37%) of participants were aged 18 -

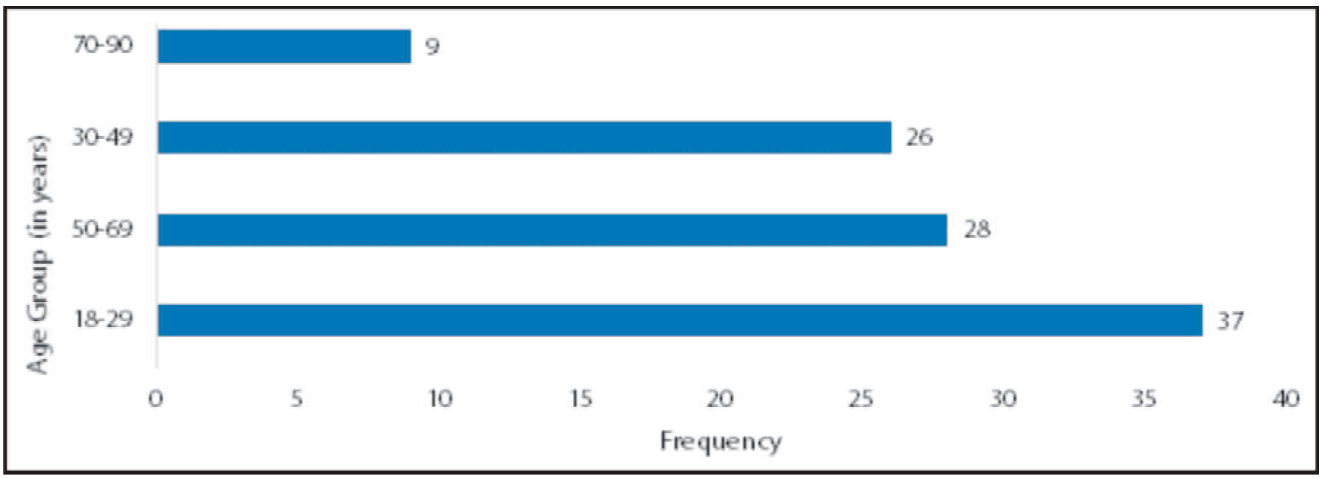

Fig. 1: *Distribution of study participants according to age: (N = 100) (Mean ± SD = 42.83 ±18.60).*

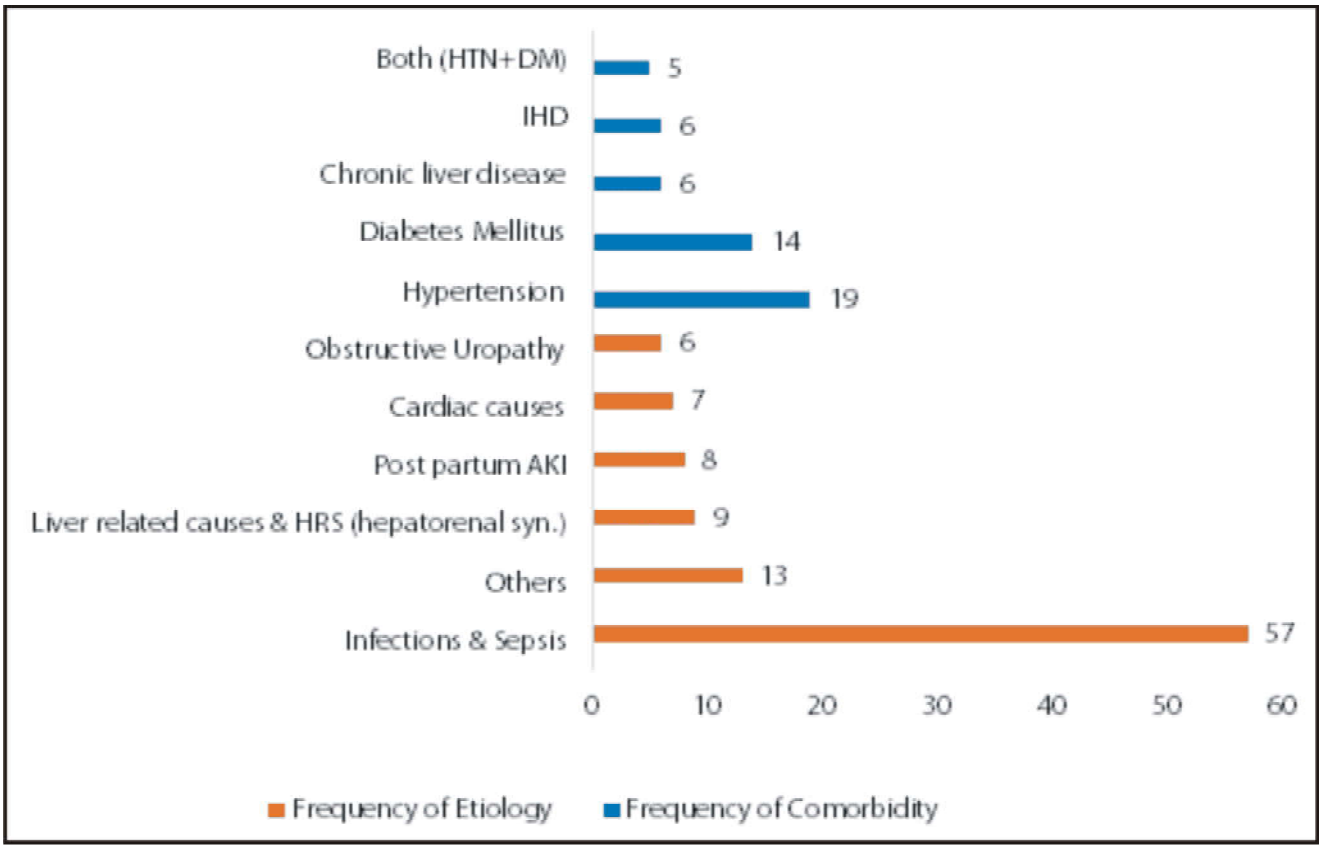

Fig. 2: *Distribution of co-morbidities and aetiologies.*

29 years, followed by 26% in the 30 - 49 age range. The mean age was 42.83 years (SD = 18.60).

Fig. 2 illustrates the distribution of co-morbidities and aetiologies associated with acute kidney injury (AKI) among the study participants. Co-morbidities were dominated by hypertension (19 cases) and diabetes mellitus (14 cases), followed by chronic liver disease and ischaemic heart disease (6 cases each), and a combination of hypertension and diabetes mellitus (5 cases).

In contrast, aetiologies were primarily linked to infections and sepsis, which accounted for the majority of cases (57), followed by other aetiologies (13), liver-related causes including hepatorenal syndrome (9), post-partum AKI (8), cardiac causes (7), and obstructive uropathy (6).

Table I: Association between different co-morbidity and outcome of acute kidney injury: (N = 100)

	Outcome			
Co-morbidity	**Recovered**	**Death**	**P value**	**95% CI**
Diabetes mellitus	8 (57.14%)	6 (42.8%)	0.076	0.1085 - 0.3529
Hypertension	14 (73.68%)	5 (26.3%)	0.793	0.273 - 0.85
Chronic liver disease	6 (100%)	0	0.1578	-
Ischaemic heart disease	6 (100%)	0	0.1578	-
Both DM+HTN	3 (60%)	2 (40%)	0.392	0.071 - 0.452

Table I shows the association between co-morbidities and AKI outcomes. While diabetes mellitus had a higher mortality rate (42.8%), the result was not statistically significant. Hypertension also did not significantly affect outcomes, and chronic liver disease and ischaemic heart disease had no recorded mortality.

Table II: Association between specific aetiology and outcome of acute kidney injury: (N = 100)

	Outcome			
Ethology	**Recovered**	**Death**	**P value**	**95% CI**
Infection and sepsis	40 (70.17%)	17 (29.8%)	0.1182	0.1702 - 0.4575
Post-partum AKI	6 (75%)	2 (25%)	0.945	0.1774 - 0.942
Obstructive Uropathy	6 (100%)	0	0.1578	-
Cardiac cause	7 (100%)	0	0.125	-
Liver-related cause	7 (77.7%)	2 (22.2%)	0.896	0.215 - 1.115
Others	10 (76.9%)	3 (23%)	0.933	0.266 - 1.060
Total	76	24		

Table II summarises the association between specific aetiologies and AKI outcomes. Infections and sepsis had the highest mortality rate (29.8%), but this was not statistically significant. Notably, patients with obstructive uropathy and cardiac-related AKI had no recorded mortality and showed favourable outcomes.

Table III: Association between infection and sepsis-related aetiology and outcome of acute kidney injury: (N = 57)

	Outcome			
Infection and sepsis	**Recovered**	**Death**	**P value**	**95% CI**
Malaria	3 (37.5%)	5 (62.5%)	0.0082	0.034 - 0.1562
Viral etiology	6 (66.6%)	3 (33.3%)	0.494	0.138 - 0.6
AGE	5 (83.3%)	1 (16.6%)	0.666	0.1798 - 1.619
LRTI	11 (78.5%)	3 (21.4%)	0.809	0.3016 - 1.184
UTI	7 (70%)	3 (30%)	0.641	0.168 - 0.710
Others	8 (80%)	2 (20%)	0.756	0.255 - 1294
Total	40	17		

Table III focuses on infection and sepsis-related aetiology, showing that malaria had the highest mortality (62.5%) among the infection subgroups, with a statistically significant p-value of 0.0082. Other infections, such as viral aetiology and urinary tract infections, showed varying outcomes, but differences were not statistically significant.

Patients who received dialysis had a significantly higher recovery rate (97.3%) compared to those who did not (68%). The mortality rate was markedly lower in the dialysis group (2.7% versus 32%), with a highly significant p-value of 0.0001 (95% CI: 2.803 - 21.8 for recovery with dialysis and 0.0059 - 0.0458 without dialysis).

Patients exposed to nephrotoxic drugs had a higher risk of developing chronic kidney disease (CKD), with 37.5% progressing to CKD compared to only 10% in the non-exposed group. Recovery rates were similar between the two groups (62.5% versus 64%). However, the association was not statistically significant (p = 0.07, 95% CI: 0.051–0.254).

Discussion

Our study found that most of the acute kidney injury (AKI) cases occurred in individuals under 60 years of age, comprising 83% of the participants, with a mean age of 42.83 years. This contrasts with studies by Nash *et al* (2002)[7] and Hsu *et al* (2007)[8], which found that AKI predominantly affected individuals over 60 years. The younger age group in our study may indicate that environmental or occupational factors, along with lifestyle choices, contribute to renal injury in this demographic population.

In present study, 60% of participants were male, while 40% were female. These findings are consistent with the study

by Prakash *et al* (2013)[9], which reported 57% males and 43% females in their cohort, with higher environmental and occupational exposures in males. The greater prevalence of AKI in males may be attributed to increased exposure to occupational risk factors and lifestyle-related kidney stressors.

Hypertension (19%) and diabetes mellitus (14%) were the most common co-morbidities among AKI patients, followed by 6% with ischaemic heart disease (IHD) and 6% with chronic liver disease. These findings are consistent with those reported by Wang *et al* (2024)[10]. The high prevalence of hypertension and diabetes highlights how chronic conditions contribute significantly to the risk of developing AKI.

Our study identified infection and sepsis (57%) as the leading causes of acute kidney injury (AKI), followed by post-partum AKI (8%), cardiac causes (7%), and liver-related causes (9%). These findings are consistent with studies by Wang *et al* (2024)[10] and Prakash *et al* (2013)[9], which similarly highlighted infections as the predominant cause of AKI, accounting for 53% and 50%, respectively, with post-partum AKI contributing 7% - 9%, cardiac causes 5% - 6%, and liver-related causes 10% - 11%. Infections, particularly in resource-limited regions, remain a major driver of AKI, underscoring the importance of timely healthcare access. Notably, respiratory tract infections (24.5%) and malaria (14%) were the most common infections in our study, which aligns with the findings of Kute *et al* (2012)[11]. Malaria and respiratory infections are thus leading causes of AKI in endemic areas.

Regarding cardiac causes, 71% of patients had ischaemic heart disease (IHD), and 29% had dilated cardiomyopathy (DCM). These findings are consistent with those of Lassnigg *et al* (2004)[12], who reported IHD in 71% of AKI patients and DCM in 31%. The link between heart disease and kidney injury, commonly referred to as cardiorenal syndrome, highlights the bidirectional nature of these conditions, where heart failure can exacerbate kidney damage.

Our study also found that disseminated intravascular coagulation (DIC) was the most frequent cause of post-partum AKI (62.5%), followed by post-partum haemorrhage (PPH) (25%). These results are similar to those of Prakash *et al* (2010)[13], who reported DIC as the leading cause of post-partum AKI in 60% of cases and PPH in 28%.

In terms of liver-related causes, hepatorenal syndrome (HRS) was the most frequent cause of AKI (44.4%), followed by acute hepatitis (22.2%). These findings are in agreement with Ginès *et al* (2009)[14], who found that HRS and acute hepatitis accounted for 45% and 20% of liver-related AKI cases, respectively. HRS is a severe complication of liver failure and often leads to kidney damage, emphasizing the need for early intervention in these cases.

Renal stones (83.3%) were the most common cause of obstructive uropathy leading to AKI, followed by neurogenic bladder (16.7%). These findings are consistent with those of Ginès *et al* (2009)[14], who reported that renal stones accounted for 75% of obstructive uropathy cases, with neurogenic bladder contributing to 25%. Timely intervention in cases of obstructive uropathy, particularly for renal stones, can prevent irreversible kidney damage and improve patient outcomes.

Our study found that 64% of patients with acute kidney injury (AKI) recovered, while 12% progressed to chronic kidney disease (CKD), and 24% died. This mortality rate is within the expected range for AKI, particularly among critically ill patients. Coca *et al* (2009)[15] reported similar findings, with 56% recovery, 15% progression to CKD, and 29% mortality in AKI patients.

When analysing recovery rates by co-morbidities, our study found that 57.14% of diabetic patients recovered, compared to 73.68% of hypertensive patients. These findings align with those of Wang *et al* (2024)[10].

Infection and sepsis-related AKI had a mortality rate of 29.8% in our study. This is similar to Bagshaw *et al* (2008)[16], who also reported a high mortality rate (35%) in sepsis-related AKI cases. Early intervention in sepsis-related AKI has been shown to reduce mortality rates, a trend confirmed by several studies.

Regarding post-partum AKI, our study found a recovery rate of 75%. Prakash *et al* (2010)[13] also reported a recovery rate of approximately 70%, reinforcing the finding that post-partum AKI generally has a favourable recovery prognosis, though a quarter of cases still result in mortality.

Malaria-related AKI had the highest mortality rate (62.5%) among infection-related aetiologies in our study, with a statistically significant p-value of 0.0082. Kute *et al* (2012)[11] found similar results, highlighting the severe impact of malaria on kidney function, especially in endemic areas.

Our research also found that mortality was significantly higher in non-dialysis patients (32%) compared to dialysis patients (2.7%), with a strong statistical correlation (p-value = 0.00001). Palevsky *et al* (2008)[17] reported that early dialysis in AKI patients significantly reduces mortality (4%), while patients without dialysis had a 30% mortality rate, a finding consistent with our results. Timely dialysis thus plays a crucial role in improving outcomes in AKI patients.

Patients exposed to potentially nephrotoxic drugs had a recovery rate of 62.5%, with 37.5% progressing to CKD. This aligns with findings by Palevsky *et al* (2008)[17], who also noted that nephrotoxic drug exposure was associated with poorer long-term kidney function, with 32% of patients developing CKD and 64% recovering. Nephrotoxic drug

exposure appears to increase the risk of CKD progression, underlining the importance of careful drug monitoring in AKI patients to prevent long-term kidney damage.

Limitations

This study being a single-centre, retrospective analysis with a focus on short-term outcomes, which may not reflect broader settings. It also lacks follow-up and causal insights, limiting generalisation and understanding of AKI's full impact.

Conclusion

This study highlights regional patterns, with younger males being predominantly affected and infections, hypertension, and diabetes as key contributors. While most recovered, diabetes increased mortality risk, and early dialysis improved survival but raised CKD incidence. Timely treatment and effective management of co-morbidities remain critical for better outcomes.

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ORIGINAL ARTICLE

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Impact of Prolonged Sitting and Shift Work on Diabetes Prevalence Among Employees in Micro, Small, and Medium Enterprises (MSMEs)

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Abstract

***Background:** The prevalence of diabetes mellitus and its associated risk factors, including work-related factors such as prolonged sitting and shift work, are significant concerns in the modern workforce. This study aimed to explore the relationship between these work-related factors and diabetes prevalence among employees.*

***Methodology:** A cross-sectional study was conducted with 200 participants aged 18 years and above. Data were collected through a structured questionnaire that captured demographic characteristics, work-related factors, health status, and lifestyle behaviours. Descriptive statistics were used to summarise the data, and logistic regression analysis was employed to assess the association between prolonged sitting, shift work, and the prevalence of diabetes, adjusted for age, gender, and physical activity levels.*

***Results:** The study population had a mean age of 42 years (SD = 9.5) with 70% males and 30% females. The average job tenure was 8 years (SD = 5.2), and the average hours spent sitting per day was 7.5 hours (SD = 2.1). The prevalence of diabetes among participants was 25% (n = 50), with 60% of those with diabetes regularly using glucose meters and an average HbA1c level of 7.5% (SD = 1.2). Logistic regression analysis revealed that prolonged sitting (OR = 1.8, 95% CI: 1.2 - 2.7, p = 0.003) and shift work (OR = 2.3, 95% CI: 1.4 - 3.7, p = 0.001) were significantly associated with an increased risk of diabetes, while other factors such as smoking and alcohol consumption were not significantly associated.*

***Conclusion:** The study highlights the significant impact of prolonged sitting and shift work on the risk of diabetes among employees. These findings underscore the importance of workplace interventions targeting these risk factors to reduce the prevalence of diabetes in the workforce.*

***Key words:** Diabetes, shift work, prolonged sitting, workplace health.*

Introduction

The rising incidence of diabetes mellitus, particularly type 2 diabetes, presents a significant global public health challenge. It is well-documented that lifestyle factors such as physical inactivity and irregular working hours significantly elevate the risk of developing diabetes[1,2]. In the context of Micro, Small, and Medium Enterprises (MSMEs), these factors are especially relevant due to the nature of the work environment. Employees in MSMEs frequently endure extended periods of sitting and are often subjected to shift work schedules, both of which are linked to adverse metabolic outcomes[3,4].

Prolonged sitting, a hallmark of many office-based jobs, is associated with numerous health issues, including obesity, cardiovascular disease, and insulin resistance[5]. Sedentary behaviour decreases muscle activity, leading to reduced glucose uptake by muscles, which in turn contributes to elevated blood glucose levels[6,7]. This issue is exacerbated in shift workers, whose circadian rhythms are disrupted, leading to hormonal imbalances that further aggravate metabolic dysregulation[8,9]. The irregular sleep patterns and altered meal timings characteristic of shift work can impair glucose metabolism and increase insulin resistance[10].

MSMEs are vital to the global economy, employing a significant proportion of the workforce, particularly in developing nations. However, despite their economic importance, workers in MSMEs often lack access to the health benefits and workplace wellness programmes more commonly available in larger corporations, making them particularly susceptible to lifestyle-related health issues, including diabetes[2]. Understanding the specific impact of prolonged sitting and shift work on diabetes prevalence in this context is crucial for developing targeted interventions to mitigate these risks.

The rationale for this study stems from the need to address the research gap concerning the unique occupational health challenges faced by MSME workers. While substantial evidence links sedentary behavior and shift work to diabetes, few studies focus specifically on the MSME sector[3,4]. Given the high prevalence of diabetes and the

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significant time MSME workers spend in sedentary and shift work conditions, this research aims to provide a clearer understanding of the associated risks and inform the development of effective prevention strategies.

The objectives of this study are to quantify the prevalence of diabetes among MSME workers and to explore the relationship between prolonged sitting, shift work, and diabetes risk[7]. By identifying the extent to which these occupational factors contribute to diabetes prevalence, this research seeks to underscore the need for tailored workplace interventions. Ultimately, the goal is to contribute to the development of evidence-based policies that promote healthier work environments in MSMEs, thereby reducing the burden of diabetes and enhancing overall workforce health.

Methodology

Study design and setting

The study employed a cross-sectional design, targeting employees from various Micro, Small, and Medium Enterprises (MSMEs) across multiple sectors. The research was conducted within office-based environments where both prolonged sitting and shift work are common. Data were collected over a three-month period, from April to June 2024. Ethical approval was secured from the Institutional Review Board of Shekhar Hospital Pvt Ltd I.E.C. approval no IEC/SH/2023/0015, and informed consent was obtained from all participants. Confidentiality of responses was maintained, and participants were informed of their right to withdraw from the study at any point.

Selection Criteria

The selection criteria for the study included employees aged 18 years and above who had been working in their current job role for a minimum of one year. Participants were required to express their willingness to provide informed consent to participate in the study. These criteria ensured that the study included individuals with sufficient exposure to the work environment under investigation, thereby enhancing the relevance and reliability of the findings.

Data sources and variables

Data was collected through a structured electronic questionnaire designed to gather comprehensive information on participants' demographic details, work-related factors, health status, and lifestyle habits. Responses were meticulously recorded in an Excel spreadsheet to facilitate analysis. The questionnaire captured variables such as age, gender, and educational level for demographic information. Work-related factors included job title, tenure with the company, hours of duty, hours spent sitting, and break times. Shift work data focused on the frequency of night shifts and the duration of shift work experience. Health status was assessed by inquiring about the presence of diabetes, use of glucose meters, frequency of blood sugar checks, and recent blood glucose and HbA1c levels. Additionally, participants' lifestyle factors were evaluated, including physical activity levels, smoking status, and alcohol consumption. The questionnaire also included questions about musculoskeletal health, specifically the presence of pain or disease involving bones, joints, or muscles. The primary outcome of interest, diabetes prevalence, was determined through self-reported data, supplemented by recent blood glucose and HbA1c levels for those who had undergone testing, as well as the use and frequency of glucose meter checks at home.

Statistical analysis

Data analysis was performed using statistical software. Descriptive statistics were used to summarise demographic characteristics, work-related factors, and health status. The prevalence of diabetes was calculated as a proportion of the total number of participants. Logistic regression analysis was conducted to examine the association between prolonged sitting, shift work, and diabetes prevalence, adjusting for potential confounders such as age, gender, and physical activity levels.

Results

Table I presents the demographic characteristics of the participants. The study included a total of 200 participants, with a mean age of 42 years (SD = 9.5). The majority of participants were male (70%, n = 140), and 30% (n = 60) were female. Most participants had a high school level of education (55%, n = 110), while 30% (n = 60) had a college degree, and 15% (n = 30) had a postgraduate degree.

Table I: Demographic characteristics

Characteristic	Number of Participants (n = 200)	Percentage (%)
Age (years)	**Mean = 42, SD = 9.5**	**–**
Gender		
– Male	140	70%
– Female	60	30%
Educational Level		
– High School	110	55%
– College	60	30%
– Post-graduate	30	15%

Table II details the work-related factors. Participants reported an average job tenure of 8 years (SD = 5.2). The average number of hours spent sitting per day were 7.5 hours (SD = 2.1), with 60% (n = 120) of participants reporting regular breaks. About 40% (n = 80) of participants engaged in shift work, with an average shift work experience of 5 years (SD = 3.8).

Table II: Work-related factors

Work-Related Factor	Number of Participants (n = 200)	Percentage (%)
Job Tenure (years)	Mean = 8, SD = 5.2	–
Hours Sitting per Day	Mean = 7.5, SD = 2.1	–
Breaks Taken		
Regular Breaks	120	60%
No Regular Breaks	80	40%
Shift Work		
Yes	80	40%
No	120	60%
Shift Work Experience	Mean = 5, SD = 3.8	-

Table III outlines the health status and lifestyle factors. The prevalence of diabetes among the participants was 25% (n = 50). Among those with diabetes, 60% (n = 30) reported regular use of glucometers, and the average HbA1c level was 7.5% (SD = 1.2). Regarding lifestyle factors, 30% (n = 60) reported engaging in regular physical activity, 20% (n = 40) were smokers, and 15% (n = 30) reported regular alcohol consumption. Additionally, 35% (n = 70) reported musculoskeletal issues.

Table III: Health status and lifestyle factors

Health Status	Number of Participants (n = 200)	Percentage (%)
Diabetes	50	25%
Regular Use of Glucose Meters	30	60% of diabetics
Average HbA1c Level	Mean = 7.5, SD = 1.2	-
Lifestyle Factors		
Regular Physical Activity	60	30%
Smoking Status	40	20%
Regular Alcohol Consumption	30	15%
Musculoskeletal Issues	70	35%

Table IV displays the logistic regression analysis results. Logistic regression analysis revealed that prolonged sitting (OR = 1.8, 95% CI: 1.2-2.7, p = 0.003) and shift work (OR = 2.3, 95% CI: 1.4-3.7, p = 0.001) were significantly associated with an increased risk of diabetes after adjusting for age, gender, and physical activity levels. Other factors such as smoking and alcohol consumption were not significantly associated with diabetes prevalence.

Table 4: Logistic regression analysis

Variable	Odds Ratio (OR)	95% CI	p-value
Prolonged Sitting	1.8	1.2-2.7	0.003
Shift Work	2.3	1.4-3.7	0.001
Physical Activity	0.7	0.4-1.2	0.18
Smoking	1.2	0.7-2.0	0.25
Alcohol Consumption	1.1	0.6-2.0	0.29

Discussion

The results of this study shed light on the significant relationship between work-related factors, particularly prolonged sitting and shift work, and the prevalence of diabetes among employees in Micro, Small, and Medium Enterprises (MSMEs). The findings are consistent with existing literature, emphasizing the critical impact of occupational factors on metabolic health.

A notable observation from this study is the prevalence of diabetes among participants, particularly those exposed to prolonged sitting and shift work. Specifically, the prevalence of diabetes was found to be 25% (50 out of 200 participants) in the overall study population. These results align with previous research that identifies sedentary behavior as a significant risk factor for developing metabolic disorders, including diabetes. Prolonged sitting has been associated with reduced muscle activity, leading to decreased glucose uptake and elevated blood glucose levels. This physiological mechanism likely contributed to the higher prevalence of diabetes observed in participants with sedentary job roles[11]. This is further supported by the meta-analysis conducted by Patterson *et al*[11], which established a clear link between sedentary behaviour and an increased risk of type 2 diabetes, highlighting the adverse effects of sedentary work environments.

Shift work also emerged as a significant factor associated with an increased risk of diabetes in this study. The prevalence of diabetes was 25% (20 out of 80 participants) among those engaged in shift work. Disruption of circadian rhythms due to shift work has been extensively documented as a contributor to hormonal imbalances, leading to impaired glucose metabolism, insulin resistance, and a heightened risk of diabetes[2,4]. The logistic regression analysis in this study underscores the significance of shift work as a predictor of diabetes, even after adjusting for confounding factors such as age, gender, and physical activity levels. Kecklund and Axelsson[12] discussed the broader health consequences of shift work, particularly insufficient sleep, which further exacerbates metabolic disruptions, increasing the risk of diabetes.

The demographic characteristics of the study population revealed that older age and lower physical activity levels were associated with a higher risk of diabetes. For instance, among participants aged 50 years and above, 50% (30 out of 60 participants) were diabetic, compared to 25% (20 out of 80 participants) among those younger than 50 years. Age is a well-established risk factor, with older adults more likely to experience impaired glucose metabolism due to physiological changes associated with aging[13]. Additionally, gender differences in diabetes risk were noted, with 26% of males (36 out of 140 participants) and 23% of females (14 out of 60 participants) being diabetic. Variations in fat distribution, hormonal regulation, and lifestyle behaviours contribute to these disparities[14]. These findings are consistent with the literature, which highlights the unique considerations and goals of diabetes care in older adults[13].

Lifestyle factors, particularly physical activity, played a protective role against diabetes in this study. Participants with higher levels of physical activity exhibited a lower prevalence of diabetes, with 18.3% (11 out of 60 participants) of active individuals being diabetic compared to 26.1% (39 out of 140 participants) among those with low physical activity levels. This aligns with existing evidence that regular physical activity enhances insulin sensitivity and improves glucose regulation[15]. However, integrating sufficient physical activity into the daily routines of employees in MSMEs remains a challenge due to work demands and sedentary job roles. The meta-analysis by Umpierre *et al*[15] underscores the importance of exercise volume in mitigating cardiometabolic risk factors, including diabetes, reinforcing the need for targeted interventions in workplace settings.

The implications of these findings are substantial for occupational health practices in MSMEs. Given the high prevalence of diabetes among workers exposed to prolonged sitting and shift work, there is a clear need for targeted interventions that promote healthier work environments. Workplace wellness programmes, ergonomic adjustments to reduce prolonged sitting, and more flexible shift schedules could play a crucial role in reducing diabetes risk. Patterson *et al*[11] suggest that interventions aimed at reducing sedentary behaviour and promoting physical activity are essential for improving metabolic health outcomes.

Limitations of the study

This study has several limitations that should be acknowledged. First, the cross-sectional design limits the ability to establish causality between work-related factors and diabetes prevalence. The reliance on self-reported data for assessing lifestyle factors, such as physical activity and sitting time, may have introduced recall bias, potentially affecting the accuracy of the findings. Additionally, the study was conducted within a specific population of MSME employees, which may limit the generalisation of the results to other occupational groups or settings. The sample size, while sufficient for identifying associations, may not have been large enough to detect more subtle effects or interactions between variables. Moreover, confounding factors such as diet, stress levels, and genetic predisposition were not thoroughly explored, which could have influenced the observed associations.

Conclusion

In conclusion, this study highlights the significant impact of occupational factors, particularly prolonged sitting and shift work, on the prevalence of diabetes among MSME employees. The findings underscore the need for targeted workplace interventions to mitigate the risk of diabetes, especially in sedentary and shift-based work environments. By promoting healthier work practices, such as reducing sitting time and optimizing shift schedules, employers can play a crucial role in improving the metabolic health of their workforce. Future research should focus on longitudinal studies to establish causal relationships and explore the effectiveness of specific workplace interventions. Additionally, a more comprehensive assessment of lifestyle and genetic factors could provide deeper insights into the complex interplay between work-related factors and diabetes risk. The outcomes of this study contribute to the growing body of evidence emphasizing the importance of addressing occupational health risks to prevent chronic diseases like diabetes.

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ORIGINAL ARTICLE

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Echocardiographic Evaluation of Diastolic Dysfunction in Asymptomatic Patients with Type 2 Diabetes Mellitus and Its Relation with HbA1c Levels

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Abstract

***Background:** Cardiovascular complications contribute as a major cause of morbidity and mortality in diabetic patients. Diastolic dysfunction (DD) is considered as an early sign of diabetic cardiomyopathy and linked to factors like duration of diabetes, insulin resistance and HbA1c levels. Diastolic dysfunction is a predictor of heart failure, making early detection and management crucial.*

***Material and Methods:** The study was conducted in the Departments of General Medicine and Cardiology at School of Medical Sciences and Research, Sharda Hospital, Greater Noida, Uttar Pradesh. 70 patients diagnosed with type 2 diabetes mellitus (DM) fulfilling the inclusion criteria were selected for the study. FBS, PPBS, HbA1c levels and other relevant parameters were studied and DD was assessed using 2-D Echocardiography.*

***Result:** The mean age of patients was 54.8 ± 11.6 years. The mean FBS, PPBS, and HbA1c were 164.4 ± 16.2 mg/dL, 223.3 ± 29.1 mg/dL, and 8.1 ± 1.6%, respectively. Out of 70 patients enrolled in the study, 36 (51.4%) had diastolic dysfunction. Patients with DD had a considerably lower E/A ratio (0.68) than patients without DD (1.04), which was statistically significant. According to the study, the longer the duration of DM, the higher was the risk of DD ($p < 0.05$).*

***Conclusion:** DD is highly prevalent in asymptomatic diabetic patients and is positively correlated with HbA1c level, obesity and the duration of diabetes. In order to delay the progression of cardiac complications, all diabetic patients should undergo regular echocardiographic evaluations for early detection of diastolic dysfunction, and necessary interventions be implemented to reduce the cardiovascular burden.*

Introduction

Diabetes Mellitus, a chronic disease is characterised by hyperglycaemia either due to relative insulin deficiency or insulin resistance. The prevalence of diabetes is rising globally, reaching epidemic proportions. 11.4% of the Indian population is estimated to have diabetes.

DM causes micro and macrovascular complications that impact almost every organ system in the body, including the heart, which contribute to its morbidity and mortality. Patients with diabetes have a much higher incidence of coronary artery disease and congestive heart failure. Compared to people without diabetes, diabetic men and women have a 3.8 and 5.5 times the relative risk of heart failure, respectively. Cardiovascular problems linked to diabetes include left ventricular dysfunction, increased left ventricular mass, increased left ventricular wall thickness, and certain diabetic cardiomyopathies[1]. Left ventricular diastolic dysfunction has been demonstrated in diabetic patients who are normotensive and have no symptoms of cardiac disease[2,3]. Increased mortality among type 2 diabetic patients with heart failure with normal ejection fraction also suggests a role for diastolic heart failure[4].

Diastolic dysfunction refers to a condition in which impairments in mechanical function are present during diastole. Both normal and impaired systolic function and the presence or absence of a clinical heart failure syndrome can cause abnormalities in diastolic function. Therefore, whereas diastolic dysfunction characterizes an aberrant mechanical property, diastolic heart failure describes the clinical condition. Numerous epidemiological, clinical, and autopsy research conducted during the past three decades have suggested that diabetic heart disease exists as a separate clinical entity. Diastolic heart failure (DHF) is also referred to as HF with retained left ventricular systolic function. Numerous investigations have shown that even in the absence of hypertension and coronary artery disease, diabetic people have a significant prevalence of heart failure. Pre-clinical diastolic dysfunction is also very common in DM subjects, according to studies[5].

Early assessment of ventricular function in diabetics is crucial because left ventricular diastolic dysfunction (LVDD) is the initial stage of diabetic cardiomyopathy that

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occurs before alterations in the systolic function[6,7]. The diastolic abnormalities are seen in diabetic patients in the absence of diabetic consequences of cardiovascular system[8,9].

Patients with diabetes have worse heart failure symptoms, take more diuretics, and have worse prognosis than people without diabetes, even though their left ventricular systolic dysfunction is similar. Diastolic dysfunction of the left ventricle in diabetes mellitus is one possible explanation for these differences. Left ventricular diastolic failure thus indicates the first stage of diabetic cardiomyopathy preceding alterations in systolic function.

An early diagnosis can be of considerable help to prevent or delay the onset of these consequences. The mortality rate from diabetes complications like infection and gangrene has gradually decreased since the invention of insulin, but the mortality rate from cardiovascular disease has gradually increased. Echocardiography offers considerable information about diastolic dysfunction and dimensions, compared to that provided by clinical evaluation. Studies support the use of echocardiography to improve patient diagnosis and management after history and physical examination[10]. The following variables are frequently measured: velocity at the mitral annulus level during early ventricular filling (e'); late ventricular filling wave (A) and ratio between the peak velocities of the early (E) and late (A) diastolic filling waves at the mitral valve (E/A ratio), isovolumetric relaxation time (IVRT), and deceleration time (DT)[11]. Accordingly, it is highly recommended to perform early detection and management of myocardial dysfunction in the diabetic population before the development of overt heart failure.

The objective of our study was to assess diastolic dysfunction in asymptomatic patients with type 2 diabetes mellitus and to find its relationship with HbA1c levels.

Material and Methods

This was a cross-sectional prevalence, analytical study conducted over a period of 18 months in a tertiary care teaching hospital in North India. Informed consent was taken from each patient. 70 patients of type 2 DM treated with oral hypoglycaemics agents and/or insulin without history suggestive of coronary heart diseases and/or congestive heart failure, attending the diabetic clinic in the department of medicine were included. Complete history and physical examination of all the patients was done and the findings were recorded. Patients with history of hypertension, thyroid disorder, chronic liver and kidney disease were excluded from the study.

Blood samples were collected to estimate FBS, PPBS, HbA1c levels, renal function tests, liver function tests and lipid profile. Cardiac evaluation was done by ECG and 2D echocardiography. Methods used to assess diastolic dysfunction were E/A ratio, left atrial size and iso-volumetric relaxation time (IVRT) on 2D echo.

The data obtained was analysed using SPSS software version 23. For each assessment point, data was statistically analysed using one way ANOVA, 't'-test and chi-square test. The level of significance was set at $p < 0.05$. Pearson correlation test was used to analyse correlation between the two variables.

Results

70 patients were enrolled in which 43 (61.4%) were males and 27 (38.6%) were females. Mean age was 54.9 years in males and 56.1 years females. Overall mean age was 54.9 ± 11.6 years. Mean body mass index (BMI) among the patients was 24.8 ± 2.9 kg/m^2, in which 18 subjects (25.7%) were overweight and 6 subjects (8.5%) were obese. Mean duration of diabetes was 7.7 ± 3.4 years. 38.6% of the subjects had diabetes duration <5 years, 44.3% had diabetes for 5 - 10 years and 17.1% had diabetes for >10 years. Mean FBS, PPBS and HbA1c among the study subjects was 164.4 ± 16.2 mg/dL, 223.3 ± 29.1 mg/dL and 8.1 ± 1.6%, respectively (Fig. 1).

36 (51.4%) patients were detected with diastolic dysfunction (DD) among the 70 patients under study. Mild diastolic dysfunction was found in 29 patients, moderate in 6 patients while 1 patient had severe dysfunction on 2D echo (Table I).

Table I: Distribution of patients according to diastolic dysfunction (DD)

Diastolic Dysfunction	Mitral E/A Ratio	Deceleration Time (m sec)	N = 70	%
Normal Function	0.75 <E/A <1.5	<220	34	48.6
Mild Dysfunction	EA ≤0.75	>220	29	41.4
Moderate Dysfunction	0.75 <E/A <1.5	150 - 200	6	8.6
Severe Dysfunction	E/A ≥1.5	<150	1	1.4

Table II shows that chances of development of diastolic dysfunction increases with the duration of diabetes ($p < 0.05$). Mean HbA1c in patients without and with DD was 6.97 ± 1.3% and 9.04 ± 1.2% respectively. Hence, HbA1c was found to be higher in subjects with DD, as compared to without DD.

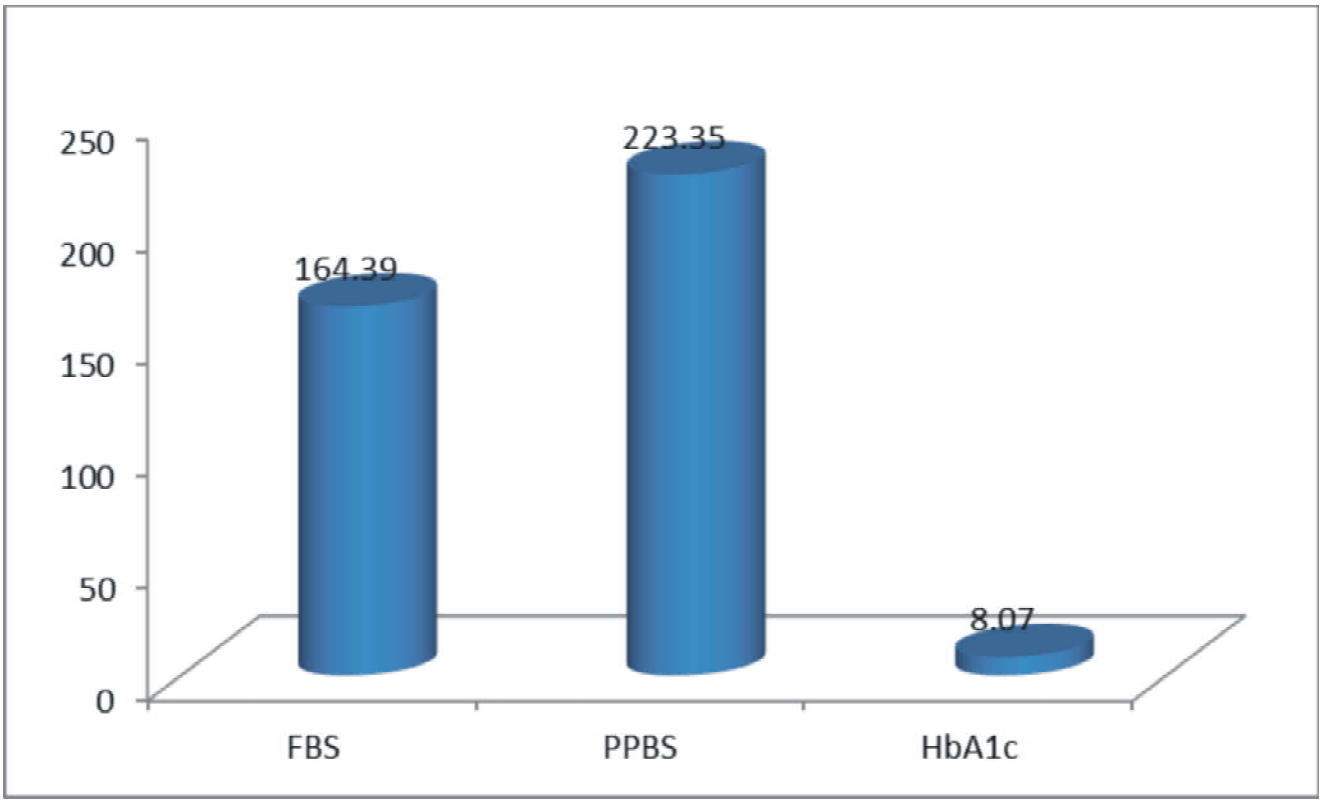

Fig. 1: *Blood glucose levels and HbA1c of patients.*

Table II: Correlation of diastolic dysfunction with duration of diabetes and HbA1c

Duration of Diabetes (in years)	Patients without DD (N = 34)		Patients with DD (N = 36)		p value
	N	%	N	%	
<5	16	47.06	8	22.22	0.005*
5 - 10	14	41.18	11	30.56	
>10	4	11.76	17	47.22	
	Mean	SD	Mean	SD	
HbA1c	6.97	1.30	9.04	1.23	0.001*

**Statistically significant.*

In our study, severity of diastolic dysfunction increased significantly with increase in HbA1c ($p < 0.05$) (Table III).

Table III: Comparison of HbA1c according to severity of diastolic dysfunction (DD)

Diastolic Dysfunction	Mean HbA1c	SD	p value
Normal Function	6.2	0.91	<0.01*
Mild Dysfunction	6.9	1.07	
Moderate Dysfunction	8.0	1.53	
Severe Dysfunction	9.0	1.67	

**Statistically significant.*

Discussion

Numerous experts have looked into how hyperglycaemia contributes to the development of diabetic cardiomyopathy. Diabetes mellitus greatly increases the risk of unfavourable cardiovascular events by causing structural and functional abnormalities that are unrelated to the effects of atherosclerosis. The toxicity of chronic hyperglycaemia in diabetes mellitus is manifested through the formation of irreversibly bound advanced glycated end products through the non-enzymatic glycation of tissue macromolecules, including proteins, lipids, and deoxyribonucleic acid (DNA). It has been discovered that these substances build up in organs like the heart. Increased apoptosis in the diabetic heart causes replacement fibrosis and connective tissue proliferation, which in turn causes increased collagen deposition in a diffused way resulting in the reduction of ventricular compliance. It has been suggested that the initial stage of the alleged "diabetic cardiomyopathy" is left ventricular diastolic dysfunction. It has been demonstrated that a lower E/A ratio is independently linked to higher cardiovascular and all-cause mortality[12,13].

In our study, 61.4% of patients were male and 38.57% were females. The average age of patients was 54.9 ± 11.6 years. In a research by Sai Vittal *et al*[14], the average age of the 50 patients was 54.1 ± 10.99 years. Sarkar *et al*[15] also found

that the majority of patients with diastolic dysfunction (80 individuals) were between the ages of 50 and 59.

65.7% of patients had normal BMI whereas 25.7% were overweight, and 8.6% were obese. The mean BMI was 24.8 ± 2.6 kg/m^2. Only 20% and 10% of the patients in a research by Jain *et al*[16] were overweight and obese, respectively, with the majority of the patients falling within the normal range. A study by Sharavanan *et al*[17], however, found that a higher percentage of patients with diastolic dysfunction were obese. According to a research by Russo *et al*, obesity and diastolic dysfunction are strongly correlated[18].

In our study out of 70 patients, 36 (51.4%) had diastolic dysfunction (DD). 41.4% had mild, 8.6% had moderate, and 1.4% had severe DD. Guria *et al*[19] studied 100 asymptomatic diabetic patients and found diastolic dysfunction in 54 (54%) patients. 4 patients had grade 3, 26 patients had grade 2, and 15 patients had grade 1 diastolic dysfunction in their study. Vittal *et al*[14] found that 66% of the patients, whereas Sharavanan *et al*[17] found that 55% of the patients had diastolic dysfunction. Diastolic dysfunction was seen in 54.33% patients with asymptomatic type 2 diabetes mellitus in a study by Patil *et al*[20]. These results were similar to that found in our study.

According to our study, the likelihood of diastolic dysfunction increases as duration of diabetes mellitus increases ($p < 0.05$). These results are in line with those of other studies. Aaron *et al* discovered a strong correlation between the duration of diabetes and the ratio of early mitral velocity E to medial mitral annulus velocity (e')[22]. Additionally, they discovered that LV diastolic dysfunction (E/e'>15) was independently linked to diabetes duration greater than 4 years. Additionally, VC Patil discovered that diastolic dysfunction was more common in patients with diabetes mellitus who had the disease for 11 - 15 years ($p < 0.05$)[20]. In another study by Bonito *et al*[23], diastolic dysfunction was found in patients with diabetes duration of less than four years and occasionally less than one year. Sarkar *et al*[15] discovered that a higher prevalence of diastolic dysfunction was linked to a longer duration of DM. Guria *et al*[19] likewise found a position correlation between DD and the duration of diabetes.

Patients with and without DD had mean HbA1c values of 9.04 ± 1.2% and 6.8 ± 1.3%, respectively. HbA1c was therefore higher in DD subjects than without it, with a statistically significant difference ($p < 0.05$). Our study found that a higher HbA1c significantly increased the degree of diastolic dysfunction ($p < 0.05$). These results are in line with a study by Hameedullah *et al*[24] who discovered a substantial association between DD and HbA1C levels. According to Guria *et al*[19], the population with LVDD had a mean HbA1c of 11.07 ± 3.66%, which was statistically significant ($p = 0.004$), compared to the population without LVDD were mean HbA1c was 9.11 ± 2.95%. This means that a patient with diabetes who has a higher HbA1c is more likely to have a higher probability of LVDD.

Similarly, the mean HbA1c of individuals with LVDD was 7.95 ± 1.09%, while that of individuals without LVDD was 7.21 ± 1.22%, according to a study of 100 cases of newly diagnosed diabetes mellitus by Srinivasa *et al*. Because the mean HbA1c of the LVDD population was greater than that of the normal LVDD population, this study also found a positive correlation between the higher HbA1c levels and the incidence of LVDD in the diabetic cohort[25]. According to a previously published study, diastolic dysfunction was observed in 9.09% of diabetic patients with an HbA1c range of 6 - 7%; 33.33% of cases with an HbA1c range of 7.1 - 8%; and 100% of cases with an HbA1c of ≥8.1%[26].

The majority of patients were on OHA or OHA with insulin when the treatment profile was assessed, and the majority of subjects had poor glycaemic control for a variety of reasons including inadequate drug dosages, poor lifestyle, poor treatment compliance, and irregular checkups. Insulin, OHA, and a combination of the two were used to treat 38.89%, 33.33%, and 27.78% of the participants with DD in this study, respectively. Insulin, OHA, and a combination of the two were administered to 32.35%, 47.06%, and 20.59% of participants without DD, respectively. In their investigation, Khade *et al*[27] found no correlation between the prevalence of diastolic dysfunction and the kind of treatment ($p = 0.27$). Compared to 23.5% of individuals on insulin and 50% of those on both insulin and OHAs, diastolic dysfunction was observed in 55.2% of patients receiving OHAs. Our findings were similar to those of Madhumathi *et al*[28], who discovered that the incidence of diastolic dysfunction was similar across different treatment groups.

This study highlights the need of early diastolic dysfunction identification as part of preventive management strategy for our diabetic patients. The higher rate of heart disease-related morbidity and mortality among diabetics necessitates the adoption of screening tests, such as echocardiograms, which are easily accessible and affordable.

Limitations of the study

1. Subclinical coronary disease was not ruled out by stress electrocardiography, stress echocardiography, myocardial perfusion imaging, or coronary angiography; and
2. Smaller sample size was studied.

Conclusion

It is clear from the discussion above that diastolic dysfunction is strongly correlated with both the duration of the diabetes mellitus and the HbA1c levels. In order to evaluate heart function for long-term therapy, it is recommended that all diabetic patients must have routine and repeated echocardiographic evaluations. Diastolic dysfunction and diabetes together can have a double-edged effect. Patients who are not diagnosed in a timely manner suffer from higher rates of morbidity and mortality. Our research highlights the necessity of using a Doppler echocardiogram to assess diabetic individuals who are frequently asymptomatic for diastolic insufficiency in order to make prompt intervention. This early diagnosis will definitely help in lowering the disease burden, as well as preventing cardiac complications.

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ORIGINAL ARTICLE

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Association of Hyperuricaemia with Urinary Albumin Excretion in Patients with Type II Diabetes Mellitus

Amit Sharma, Praveen Kumar Malik**, Rajesh Manocha***, Ravi Bhargav*****

Abstract

***Background:** Diabetes mellitus (DM) is a major global health concern, leading to numerous complications, including retinopathy, neuropathy and nephropathy. Hyperuricaemia and glycated haemoglobin (HbA1c) have been identified as potential contributors to diabetic nephropathy, yet their combined impact on urinary albumin excretion (UAE) is not fully understood. The interplay between these factors may provide critical insights into early detection and management strategies for diabetic nephropathy.*

***Objective:** This study aims to investigate the relationship between serum uric acid and UAE in patients with type II diabetes mellitus (T2DM), and to determine whether hyperuricaemia and glycaemic control influence the severity of albuminuria.*

***Methods:** A hospital-based cross-sectional study was conducted among 150 T2DM patients, measuring serum uric acid, HbA1c, and urinary albumin levels. Statistical analyses, including correlation and regression models, were used to assess relationships between these variables.*

***Results:** Higher serum uric acid level was significantly associated with increased UAE. Patients with elevated uric acid levels had a higher risk of moderately and severely increased albuminuria. A combined effect of hyperuricaemia and poor glycaemic control was observed, leading to a greater likelihood of progressive kidney dysfunction.*

***Conclusion:** Both hyperuricaemia and poor glycaemic control independently contribute to increased UAE, highlighting their importance as early indicators of diabetic nephropathy. Proactive management of uric acid levels and HbA1c may help in reducing the risk of renal complications in T2DM patients.*

***Key words:** Diabetes mellitus, hyperuricaemia, HbA1c, urinary albumin excretion, diabetic nephropathy.*

Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder characterised by persistent hyperglycaemia due to insulin resistance, insufficient insulin secretion, or both. It has emerged as a global health crisis, with increasing prevalence and significant morbidity and mortality. Among the myriad complications associated with DM, diabetic nephropathy is a leading cause of end-stage renal disease (ESRD), imposing a substantial burden on healthcare systems worldwide. Early detection and intervention are paramount to slowing disease progression and mitigating long-term renal damage[1].

One of the most commonly used markers for diabetic nephropathy is urinary albumin-creatinine ratio (UACR), which serves as an early indicator of renal dysfunction. Moderately increased albuminuria, defined as UACR between 30 and 300 mg/g, represents the initial stage of kidney damage, whereas severely increased albuminuria, exceeding 300 mg/g, suggests advanced renal impairment. Understanding the factors that contribute to increased UACR in diabetics is crucial for implementing timely and effective treatment strategies[2].

Hyperuricaemia, or elevated serum uric acid levels (>7.0 mg/dL in men and >5.7 mg/dL in women), has gained attention as a potential contributor to renal dysfunction. Uric acid has been implicated in endothelial dysfunction, oxidative stress, and inflammatory responses, all of which can exacerbate kidney damage in diabetics. Additionally, poor glycaemic control, as indicated by elevated HbA1c levels, is strongly associated with renal impairment due to the damaging effects of prolonged hyperglycaemia on the renal microvasculature. However, the combined impact of hyperuricaemia and glycaemic control on UACR remains underexplored[3].

This study aims to investigate the association between serum uric acid and urinary albumin excretion in T2DM patients. By identifying these relationships, we hope to contribute valuable insights into the early detection and management of diabetic nephropathy, ultimately improving patient outcomes.

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Methods

Study Design and Participants

This hospital-based cross-sectional study was conducted at ESIC Medical College and Hospital, Faridabad, involving T2DM patients aged 18 - 65 years. The study included individuals diagnosed with T2DM for at least one year, as confirmed by their medical history and laboratory reports. Patients with chronic kidney disease (CKD), acute infections, or those on medications influencing uric acid metabolism, such as diuretics or uricosuric agents, were excluded to minimise confounding variables.

A structured questionnaire was used to collect demographic and clinical data, including age, gender, duration of diabetes, lifestyle habits, medication history, and co-morbid conditions such as hypertension and dyslipidaemia. A thorough physical examination was performed, including measurements of blood pressure, and body mass index (BMI).

Data Collection and Laboratory Analysis

Blood and urine samples were collected. Laboratory tests were conducted using standardised protocols:

- Serum Uric Acid: Measured using reflectance spectrophotometry. Hyperuricaemia was defined as >7.0 mg/dL in men and >5.7 mg/dL in women.
- HbA1c: Assessed by using immunoturbidimetry, with a cut-off value of >6.5% for poor glycaemic control.
- Urinary Albumin Creatinine Ratio: Determined via reflectance spectrophotometry. Spot urine samples were collected. Patients were classified as normoalbuminuric (<30 mg/g), moderately increased albuminuric (30 - 300 mg/g), or severely increased albuminuric (>300 mg/g).
- Serum Creatinine and eGFR: Measured to assess baseline renal function and estimated glomerular filtration rate (eGFR).

Statistical Analysis

Descriptive statistics were used to summarise baseline characteristics. Pearson's correlation was employed to assess the association between uric acid, HbA1c, and UACR. A multiple regression model was used to adjust for confounders such as age, BMI, hypertension, and dyslipidaemia. Statistical significance was set at $p < 0.05$.

Results

Table I categorises the age distribution of a group of 150 participants. The majority of the participants were between the age of 31 - 60 years, accounting for 63.4% of the study cohort. The second largest age group was ≥60 years of age, representing 28% of the sample. Those aged ≤30 years made up 8.6% of the study group. Overall, the mean age of the group was 40.3 ± 14.5 years.

Table I: Distribution of age

Age (Years)	Frequency	% of Total
≤30	13	8.6%
31 - 60	95	63.40%
≥60	42	28%
Total	150	100.0%
Mean ± SD	40.3 ± 14.5	

$X^2 = 25.1$, $p = <0.001$

Table II: Distribution of gender

Gender	Frequency	% of Total
Male	67	44.7%
Female	83	55.3%
Total	150	100.0%

$X^2 = 1.71$, $p = 0.191$

Table II displays the gender distribution of patients with type II diabetes mellitus, showing a slight predominance of females over males. Out of 150 participants, 55.3% were females (n = 83), while males accounted for 44.7% (n = 67). This distribution indicated a minor gender imbalance, with females being more represented in the study sample. A chi-square test was conducted to examine whether this distribution was significantly different from an expected equal proportion of genders. The chi-square value ($\chi^2 = 1.71$) and the associated p-value ($p = 0.191$) indicated no statistically significant difference in gender distribution, suggesting that the observed variation could likely be due to random chance rather than a true gender disparity in the sample.

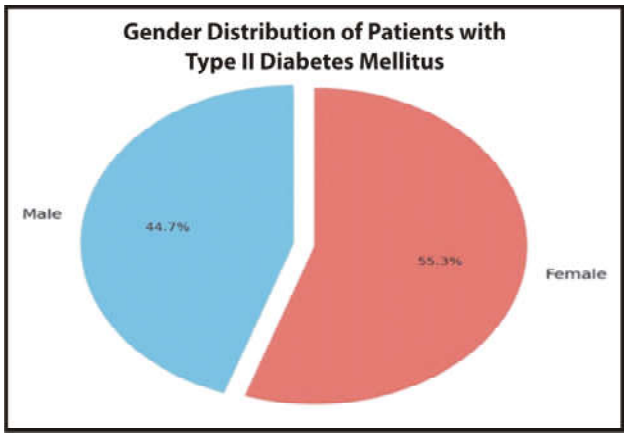

Fig. 1:

Table III: Distribution of chief complaints

Chief Complaints	Frequency	% of Total
Fatigue	31	20.66%
Weight loss	43	28.7%
Increased thirst	36	24.0%
Frequent urination	25	16.64%
Others	15	10.0%
Total	150	100.0%

$X^2 = 3.33, p = 0.343$

In the study analyzing chief complaints among 150 patients, the most common complaint reported was weight loss, affecting 43 individuals and constituting 28.7% of the total complaints. Increased thirst followed closely, reported by 36 patients, accounting for 24.0% of the complaints. Fatigue was another significant complaint, experienced by 31 patients, making up 20.66% of the total. Frequent urination was noted in 25 patients, representing 16.64% of the complaints. Other less common complaints were grouped under 'Others,' totaling 15 cases and covering 10.0% of the complaints (Table III).

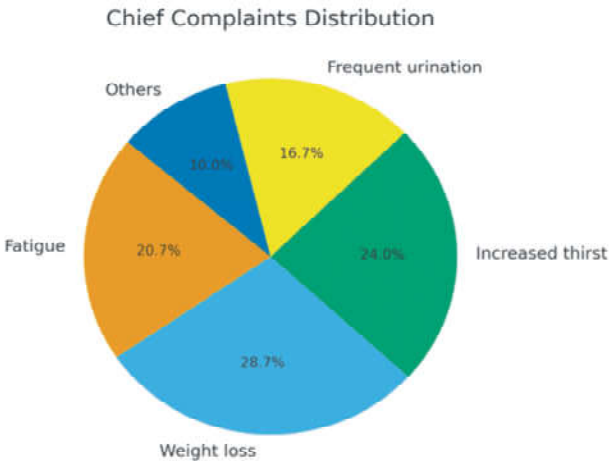

Fig. 2:

Table IV: Descriptive statistics of vital signs

	95% Confidence Interval					
Vital signs	Mean	Lower	Upper	SD	t-value	p-value
SBP (mmHg)	135.7	124	158	17.12	97.1	0.00238
DBP (mmHg)	85.1	82	98	7.15	145.9	0.00515
Pulse (/min)	79.3	73	109	12.83	75.7	0.00434
Respiratory Rate (/min)	15.6	13	16	2.34	81.3	0.00276

Table IV data represents vital signs with their respective mean values, 95% confidence intervals, standard deviations, t-values, and p-values. The systolic blood pressure (SBP) had a mean of 135.7 mmHg with a 95% confidence interval ranging from 124 to 158 mmHg, a standard deviation of 17.12, a t-value of 97.1, and a highly significant p-value of 0.00238. Diastolic blood pressure (DBP) showed a mean of 85.1 mmHg, a confidence interval from 82 to 98 mmHg, a standard deviation of 7.15, a t-value of 145.9, and a p-value of 0.00515. The pulse rate was observed at a mean of 79.3 beats per minute, with a confidence interval between 73 and 109, a standard deviation of 12.83, a t-value of 75.7, and a p-value of 0.00434. Lastly, the respiratory rate was reported with a mean of 15.6 breaths per minute, a confidence interval from 13 to 16, a standard deviation of 2.34, a t-value of 81.3, and a p-value of 0.00276. This statistical data indicates highly significant differences for all measured vital parameters.

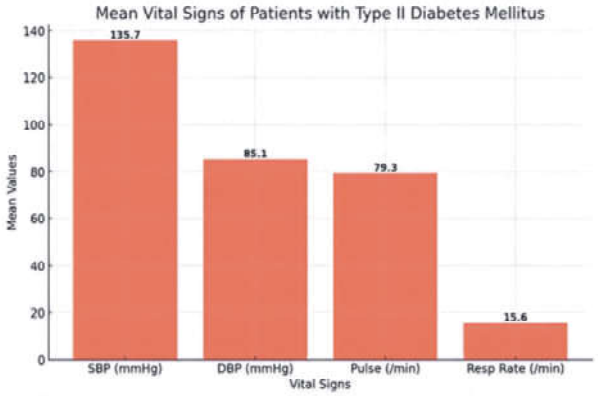

Fig. 3:

Table V: Descriptive statistics of Renal Function Tests (RFT)

	95% Confidence Interval					
RFT	Mean	Lower	Upper	SD	t-value	p-value
Blood Urea (mg/dl)	33.673	22.20	48.52	9.861	41.8	0.00532
Creatinine (mg/dl)	0.897	0.6	0.98	0.186	59	0.0012
Uric Acid (mg/dl)						
– Male	10.532	7.1	11.2	1.392	60.9	0.053
– Female	9.231	6.2	10.7	1.235	58.2	0.00123

Table V depicts the assessment of renal functions through blood tests, and the results show the following statistics within a 95% confidence interval. For blood urea, the mean level was 33.673 mg/dL, ranging from 22.20 to 48.52 mg/dL with a standard deviation (SD) of 9.861, a t-value of 41.8, and a p-value of 0.00532, indicating statistical significance. Creatinine level had a mean of 0.897 mg/dL, with a lower limit of 0.6 mg/dL and an upper limit of 0.98 mg/dL, an SD of 0.186, a t-value of 59, and a highly significant p-value of 0.0012. Uric

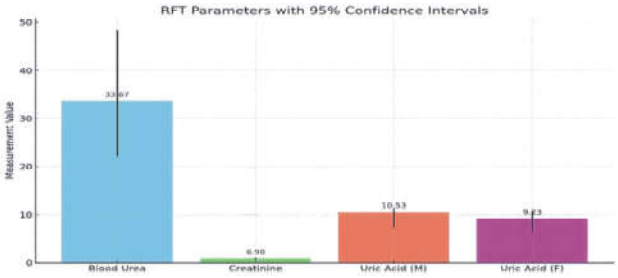

Fig. 4:

acid levels varied by gender; males had a mean of 10.532 mg/dL with a range of 7.1 to 11.2 mg/dL, an SD of 1.392, a t-value of 60.9, and a p-value of 0.053, suggesting marginal significance. In contrast, females had a mean uric acid level of 9.231 mg/dL, ranging from 6.2 to 10.7 mg/dL, an SD of 1.235, a t-value of 58.2, and a p-value of 0.00123, also indicating statistical significance.

Table VI: Descriptive statistics of glycaemic control

		95% Confidence Interval				
Glycaemic Control	**Mean**	**Lower**	**Upper**	**SD**	**t-value**	**p-value**
HbA1C (%)	7.64	7.6	9.8	1.53	53.2	0.0017
RBS (mg/dl)	295.53	286	347	56.6	63.9	0.0053
FBS (mg/dl)	190.85	180	221	33.38	70	0.0062

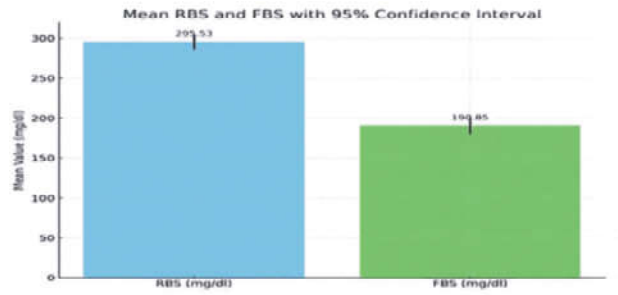

Fig. 5:

Table VI describes the glycaemic control parameters, as measured in the study, exhibiting significant differences. The mean haemoglobin A1C (HbA1C) was 7.64% with a 95% confidence interval (CI) ranging from 7.6% to 9.8%, standard deviation (SD) of 1.53%, and a highly significant t-value of 53.2 (p - 0.0017). Random blood sugar (RBS) levels had a mean of 295.53 mg/dL, with a 95% CI of 286 to 347 mg/dL, SD of 56.6 mg/dL, and a t-value of 63.9 (p 0.0053). Fasting blood sugar (FBS) levels were averaged at 190.85 mg/dL, with a 95% CI from 180 to 221 mg/dL, SD of 33.38 mg/dL, and a t-value of 70 (p-0.0062), indicating strong statistical significance in all measurements of glycaemic control within the study.

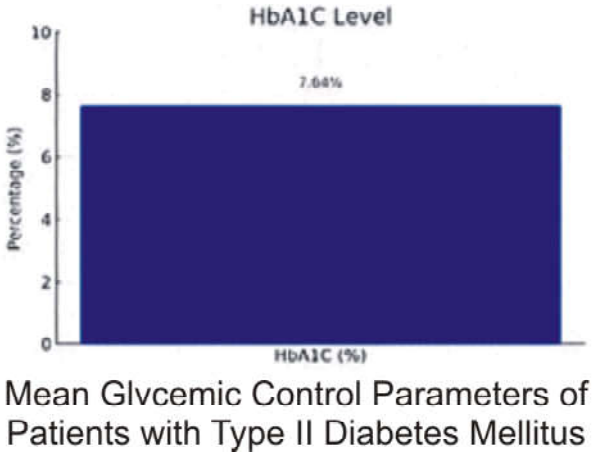

Fig. 6:

Table VII: Distribution of UACR category with age

Age (years) with frequency	**Normal Albuminuria**	**Moderately Increased Albuminuria**	**Severely Increased Albuminuria**
<30 (13)	7	4	2
30 - 60 (95)	22	44	29
>60 (42)	2	4	36
Total = 150	31	52	67

$X^2 = 29.0$, $p = <0.001$.

Table VII categorises albuminuria into three UACR categories: normal albuminuria, moderately increased albuminuria, and severely increased albuminuria. Normal albuminuria was observed in 31 patients, accounting for 20.66% of the total. Moderately increased albuminuria was more frequent, observed in 52 patients, comprising 34.67% of the total. The highest frequency was seen in severely increased albuminuria, with 67 patients, making up 44.67% of the total. among the studied group. The highest frequency of

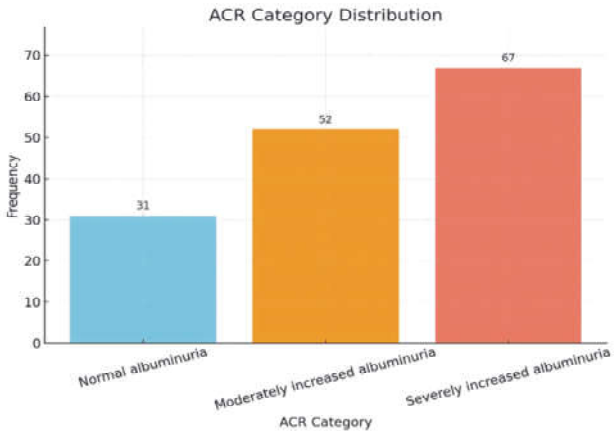

Fig. 7:

moderately and severely increased albuminuria was observed in age group 30 - 60 yrs and >60 yrs, respectively.

Table VIII depicts the logistic regression analysis, and the impact of various predictors on the urinary albumin creatinine ratio (UACR). The haemoglobin A1c (HbA1C) levels had a positive association with an increase in the UACR, with an odds ratio (OR) of 1.57 (95% CI: 1.22, 2.02) per percentage increase, indicating a statistically significant effect (p <0.001). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) also showed positive effects with ORs of 1.02 (95% CI: 1.00, 1.04) and 1.03 (95% CI: 1.01, 1.05) per mmHg increase respectively, achieving significance at p-values of 0.045 and 0.021. Age demonstrated a positive effect on UACR category with an OR of 1.05 per year increase (95% CI: 1.01, 1.09; p = 0.012). Creatinine levels were strongly associated with UACR category, with an OR of 2.41 (95% CI: 1.43, 4.05) per mg/dL increase (p <0.001). Uric acid levels also contributed positively to the UACR category with an OR of 1.36 (95% CI: 1.02, 1.82) per mg/dL increase (p = 0.038).

Table VIII: Impact of various predictors on UACR using logistic regression

Model Co-efficients - UACR Category

						95% Confidence Interval	
Predictor	**Estimate**	**SE**	**Z**	**P**	**Odds ratio**	**Lower**	**Upper**
HbA1C (%)	0.45	0.12	3.75	<0.001	1.57	1.22	2.02
SBP (mmHg)	0.02	0.01	2.00	0.045	1.02	1.00	1.04
DBP (mmHg)	0.03	0.01	2.30	0.021	1.03	1.01	1.05
Age	0.05	0.02	2.50	0.012	1.05	1.01	1.09
Creatinine (mg/dL)	0.88	0.26	3.38	<0.001	2.41	1.43	4.05
Uric Acid (mg/dL)	0.31	0.15	2.07	0.038	1.36	1.02	1.82

SE: Standard Error, Z: Z-Value, p = p-Value

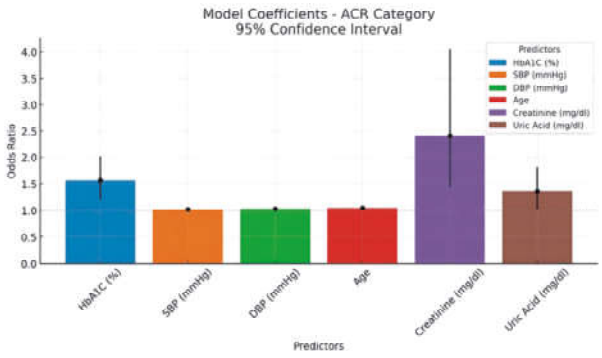

Fig. 8:

Discussion

The present study demonstrated a significant association between age and urinary albumin excretion in type II diabetes mellitus patients. The highest frequency of severely increased albuminuria was observed in the >60 year age group, accounting for 36 out of the 150 participants. Additionally, the 30 - 60 year age group also showed considerable moderately increased albuminuria, i.e., 44 out of 150 patients. The mean age of participants was 40.3 ± 14.5 years. Statistical analysis highlighted this age-related trend in albumin excretion, evidenced by a significant chi-square value of 29.0 and a p-value of less than 0.001. Neupane *et al*[4] reported a mean age of 58.94 years with a standard deviation of 13.80 years among their diabetic cohort. Their study primarily focused on older individuals compared to our study, where a broader age range was considered. Despite the differences in age distribution, both studies underscore the prevalence of kidney-related complications in older diabetic patients. Kaushal *et al*[5] analysed 100 patients with a mean age of 57.64 years and a standard deviation of 10.07, with age ranging from 40 to 80 years. This narrower age range and higher mean age compared to our study indicates focus on a relatively old demography. Similar to our findings, Kaushal *et al* study observed the increased renal stress among older diabetic patients, though direct comparisons on urinary albumin excretion were limited without specific albuminuria data from their study.

The present study identified a gender distribution among type II diabetes mellitus patients with 55.3% female (83/150) and 44.7% male (67/150). The chi-square analysis showed no significant gender difference in urinary albumin excretion, with a value of 1.71 and a p-value of 0.191. Neupane *et al*[4] reported a gender distribution of 58% male (29 participants) and 42% female (21 participants) in their diabetic cohort. This distribution differs slightly from our study, where a higher proportion of females was noted. Kaushal *et al*[5] analysed a cohort where males comprised

52% and females 48%, which is more balanced compared to our study but still shows a slight male predominance, contrasting with our female-majority findings.

The present study investigated chief complaints among 150 type II diabetes mellitus (T2DM) patients, revealing that increased thirst (24.0%) and weight loss (28.7%) were the most common, followed by fatigue (20.66%), frequent urination (16.64%) and other less common were grouped under "others" covering 10% of the complaints. A chi-square test yielded a value of 3.33 with a p-value of 0.343, indicating no significant variation in the distribution of these symptoms among the participants. Wongkongkam *et al*[6] assessed clinical presentations in T2DM patients with and without peripheral arterial disease (PAD). Among their participants, those with PAD often reported intermittent claudication (70.4%), while a significant majority of those without PAD had no symptoms (90%). This contrasts starkly with the frequent general diabetic symptoms like fatigue and weight loss noted in our study. Their chi-square analysis showed a highly significant difference in symptom presentation ($p \leq 0.001$), emphasizing the impact of PAD on symptom severity and type in diabetic patients. Hamiel and Zeitler[7] detailed the clinical presentations of type 1 and type 2 diabetes in children. Common symptoms for both T1DM and T2DM included polydipsia, polyuria, and polyphagia. T2DM in children was often diagnosed incidentally and associated with obesity, acanthosis nigricans, and more commonly, co-morbidities like hypertension and dyslipidaemia. While their study focuses on a younger demography and differentiates by diabetes type, the presence of symptoms such as polydipsia and polyuria align with our findings in an adult T2DM population.

The present study assessed the vital parameters of patients with type II diabetes mellitus, establishing significant findings for systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, and respiratory rate. The mean SBP was reported at 135.7 mmHg with a confidence interval (CI) of 124 to 158 mmHg, and a standard deviation (SD) of 17.12 mmHg. DBP averaged 85.1 mmHg with a CI of 82 to 98 mmHg and an SD of 7.15 mmHg. The pulse rate was 79.3 per minute with a CI of 73 to 109 per minute and an SD of 12.83 per minute, while the respiratory rate was 15.6 per minute with a CI of 13 to 16 per minute and an SD of 2.34 per minute. Each parameter showed a highly significant t value (SBP: 97.1, DBP: 145.9, Pulse: 75.7, Resp Rate: 81.3) with p-values of 0.00238, 0.00515, 0.00434, and 0.00276, respectively, indicating robust statistical significance across all measures. Kaushal *et al*[5] reported mean SBP and DBP values of 128.96 mmHg (SD 14.62) and 77.1 mmHg (SD 7.53), respectively, in a cohort of 100 participants. The maximum and minimum reported SBP values were 160 and 110 mmHg, while for DBP, they were 90 and 60 mmHg. These results show lower average blood pressures compared to our findings, possibly indicating differences in demographic characteristics or disease management strategies between the cohorts. Lai *et al*[8] examined systolic and diastolic blood pressures in participants with and without albuminuria. Their findings showed mean SBP values of 133.91 mmHg (SD 16.20) for those without albuminuria and 134.80 mmHg (SD 15.77) for those with albuminuria, with a hazard ratio of 1.01 (95% CI: 0.98 - 1.04, $p = 0.40$). For DBP, the means were 77.57 mmHg (SD 10.85) without albuminuria and 76.45 mmHg (SD 11.06) with albuminuria, with a hazard ratio of 0.99 (95% CI: 0.96 - 1.04, $p = 0.72$). These blood pressure values are also lower than those observed in our study, and the statistical analysis did not demonstrate significant differences associated with albuminuria, contrasting with the significant trends observed in our data.

The present study assessed renal function tests (RFT) in patients with type II diabetes mellitus, showing significant results for blood urea, creatinine, and uric acid levels. The mean values were 33.673 mg/dL for blood urea with a confidence interval (CI) of 22.20 to 48.52 and a standard deviation (SD) of 9.861, creatinine was 0.897 mg/dL with a CI of 0.6 to 0.98 and an SD of 0.186, and uric acid in males 10.532 mg/dL with a CI of 7.1 to 11.2, SD of 1.392 and in females mean 9.231 with a CI of 6.2 to 10.7 and a SD of 1.235. All parameters showed high statistical significance with t-values exceeding 40 and p-values of 0.00532, 0.0012, 0.053, and 0.00123, respectively. Qin *et al*[9] examined serum uric acid (SUA) levels in a cohort differentiated by gender, reporting mean SUA of 303.6 μmol/L in total, with males at 321.4 μmol/L and females at 275.8 μmol/L. The study highlighted significant differences between genders ($p < 0.0001$). The uric acid level reported by Qin *et al*[9] when converted to mg/dL (divide by 59.48 to convert μmol/L to mg/dL) would be approximately 5.10 mg/dL for the total group, which is lower compared to the uric acid levels found in our study. Nikolaidou *et al*[10] analysed urea, creatinine, and uric acid in diabetic patients with recent onset, where urea averaged 31.2 mg/dL (± 6.9 SD), creatinine 0.88 mg/dL (±0.16 SD), and uric acid 5.4 mg/dL (± 1.7 SD). Their findings are comparable to ours, although the creatinine and uric acid levels in our study are slightly higher. No significant differences were found in urea and creatinine levels between hypertensive and normotensive diabetic patients, nor in uric acid levels (p-values: urea = 0.927, creatinine = 0.114, uric acid = 0.458).

The present study evaluated glycaemic control in patients with type II diabetes mellitus, achieving significant findings in HbA1C, random blood sugar (RBS), and fasting blood sugar (FBS). The study reported a mean HbA1C of 7.64%

with a confidence interval (CI) of 7.6% to 9.8% and a standard deviation (SD) of 1.53%, RBS at 295.53 mg/dL (CI: 286 to 347, SD: 56.6), and FBS at 190.85 mg/dL (CI: 180 to 221, SD: 33.38). All parameters indicated highly significant statistical values with t-values over 50 and p-values 0.0017, 0.0053 and 0.0062, respectively. Bonakdaran *et al*[11] reported higher mean values in their diabetic cohort with a fasting blood glucose of 191.32 mg/dL (SD: 66.25) and an HbA1C of 8.68% (SD: 1.96), both higher than in our study. This suggests worse glycaemic control in their sample as compared to ours, where the mean HbA1C was notably lower at 7.64%. Neupane *et al*[4] also found a higher average of HbA1C at 8.12% with an SD of 2.14%, which again indicates less effective glycaemic control compared to our study's findings. The higher variability in their data suggests a broader range of control among participants. Sabzghabaei and Rajabian[12] reported mean fasting blood glucose at 139.84 mg/dL (SD: 38.4) and HbA1C at 7.41% (SD: 1.41), which are both lower than in our study. Their lower FBS and HbA1C readings indicate better average glycaemic control among their participants compared to our study. These comparative insights underline the variability in diabetes management effectiveness across different populations, stressing the importance of tailored treatment approaches to optimise glycaemic control.

In the present study, we analysed the distribution of albuminuria among 150 patients with type II diabetes mellitus, categorizing them based on albumin creatinine ratio (ACR). The results demonstrated that 20.66% (31 patients) had normal albuminuria, while 34.67% (52 patients) exhibited moderately increased albuminuria and severely increased albuminuria was in 44.67% (67 patients). The chi-square statistic was significant at 29.0 with a p-value of less than 0.001, indicating a significant distribution of albuminuria categories among the participants. Kaushal *et al*[5] categorised diabetic patients into groups based on their ACR levels. They reported a mean urinary ACR of 22.3 µg/mg (SD: 4.53, range: 14 - 30) for the normoalbuminuria group (46 patients), 144.6 µg/mg (SD: 71.11, range: 56.2 - 380) for the moderately increased albuminuria group (33 patients), and 421.3 µg/mg (SD: 150.33, range: 51.8 - 750) for the severely increased albuminuria group (21 patients). The higher ACR values in their moderately increased albuminuria and severely increased albuminuria groups compared to our study highlight more pronounced renal involvement. These studies collectively underscore the significance of assessing albuminuria in diabetes management, demonstrating variations in kidney health across different diabetic cohorts and reinforcing the importance of early detection and intervention.

The present study investigated the association between several predictors and albuminuria category in patients with type II diabetes mellitus using logistic regression analysis. Significant findings were observed for the intercept and HbA1C, with the latter showing a substantial influence on the odds of having albuminuria: for each percentage increase in HbA1C, the odds of albuminuria increased by approximately 1.57 times (Odds Ratio: 1.57, CI: 1.22 - 2.02, p <0.001). SBP and DBP also showed positive effects with ORs of 1.02 (95% CI: 1.00, 1.04) and 1.03 (95% CI: 1.01, 1.05) per mmHg increase respectively, achieving significance at p-values of 0.045 and 0.021. Age demonstrated a positive effect on ACR category with an OR of 1.05 per year increase (95% CI: 1.01, 1.09; p = 0.012). Creatinine levels were strongly associated with ACR category, with an OR 2.41 (95% CI: 1.43, 4.05) per mg/dL increase (p <0.001). Uric acid levels also contributed positively to ACR Category with an OR of 1.36 (95% CI: 1.02, 1.82) per mg/dL increase (p = 0.038). These predictors showed significant associations with albuminuria in this cohort.

In patients with elevated levels of uric acid (UA), there is often an associated increase in urinary albumin-to-creatinine ratio (UACR), indicating a potential for kidney damage or disease progression. Similarly, heightened levels of HbA1C, a marker for long-term glycaemic control, are linked to increased UACR, reflecting a higher risk of diabetic kidney disease. When both uric acid and HbA1C levels are elevated, the impact on UACR is even more pronounced. This dual elevation exacerbates the stress on the kidneys, potentially accelerating the pathogenesis of kidney damage. Therefore, monitoring and managing both uric acid and HbA1C levels in patients are crucial for mitigating the risk of renal complications, especially in those with predisposing conditions such as diabetes and hyperuricaemia.

Conclusion

This study highlights a significant association between hyperuricaemia, glycaemic control, and urinary albumin excretion in T2DM patients. Elevated serum uric acid and HbA1c independently contribute to increased UAE, suggesting their potential role as early biomarkers of diabetic nephropathy. The combined effect of hyperuricaemia and poor glycaemic control accelerates renal dysfunction, emphasizing the need for comprehensive management strategies targeting both metabolic and renal parameters.

From a clinical perspective, early screening for serum uric acid and HbA1c levels in diabetic patients could facilitate timely interventions, potentially delaying or preventing the onset of diabetic nephropathy. Given that hyperuricaemia has been linked to endothelial dysfunction and oxidative stress, uric acid-lowering therapies such as allopurinol or febuxostat may serve as adjuncts to conventional

nephroprotective strategies. Additionally, strict glycaemic control through lifestyle modifications and pharmacologic interventions remain paramount in mitigating kidney damage.

Despite these promising findings, certain limitations should be acknowledged. The study's cross-sectional design precludes establishing causality, and the relatively small sample size necessitates larger-scale longitudinal studies for validation. Moreover, factors such as dietary patterns, genetic predisposition, and inflammatory markers warrant further exploration to elucidate their role in the observed associations.

In conclusion, integrating serum uric acid and HbA1c measurements into routine diabetic care may enhance early detection and personalised management of diabetic nephropathy. Future research should aim to establish causative relationships and evaluate the efficacy of targeted interventions in improving renal outcomes in T2DM patients.

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ORIGINAL ARTICLE

JIACM 2025; 26 (3): 121-25

A Comparative Study of Therapeutic Effects of Plasma Exchange and Intravenous Immunoglobulins in Guillain Barre Syndrome

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Abstract

***Background:** Guillain-Barré Syndrome (GBS), a rare but significant cause of acute flaccid paralysis, exhibits diverse clinical presentations ranging from symmetrical limb weakness to cranial nerve involvement and autonomic dysfunction. Therapeutic options include plasma exchange (PE) and intravenous immunoglobulin (IVIg), both shown to improve outcomes. However, limited data exist on the comparative effectiveness and outcomes of these therapies in the Indian population.*

***Materials and Methods:** This retrospective, observational study was conducted at a tertiary care hospital in South Gujarat from July 2020 to February 2023. A total of 100 patients diagnosed with GBS were included, 50 each in the PE and IVIg groups. Data was collected using medical records, with clinical and diagnostic evaluations based on the Brighton Criteria. Outcomes were assessed using the Hughes Disability Scale. Statistical analyses were performed using Epi Info software.*

***Results:** The cohort comprised of 65% males, with a mean age of 31.5 ± 4.1 years in the IVIg group and 36.0 ± 2.8 years in the PE group. Demyelinating neuropathy was the most common subtype (68%). At four weeks post-therapy, the PE group demonstrated significantly better improvement in disability scores (mean 1.31 ± 0.16 versus 2.29 ± 0.27, p = 0.001) and a shorter weaning duration from mechanical ventilation (19.1 ± 3.5 days versus 37.7 ± 5.8 days, p = 0.04). Mortality was significantly lower in the PE group (8% versus 32%, p = 0.003).*

***Conclusion:** PE outperformed IVIg in improving functional outcomes and reducing mortality in GBS patients. These findings underscore the need for evidence-based allocation of resources, particularly in resource-constrained settings.*

***Key words:** Guillain-Barré Syndrome (GBS), Plasma Exchange (PE), Intravenous Immunoglobulin (IVIg), Acute Flaccid Paralysis, Disability Outcomes.*

Introduction

Guillain-Barré Syndrome (GBS) is a leading cause of acute flaccid paralysis, presenting with symmetrical limb weakness and hypo- or areflexia, typically progressing to maximum severity within four weeks[1]. Sensory symptoms, such as paraesthesia and numbness, generally follow a symmetrical distal pattern. The most prevalent subtypes of GBS include acute inflammatory demyelinating polyneuropathy (AIDP) and acute motor axonal neuropathy (AMAN), with Miller Fisher syndrome (MFS), characterised by ophthalmoplegia, ataxia, and areflexia, being a less common variant[2]. The clinical course and outcomes of GBS can vary widely[2].

GBS is a rare condition, with an incidence ranging from 0.81 to 1.89 (median 1.11) per 100,000 person-years. It is more common in men than women (3:2 ratio). Global incidence rates vary, from as low as 0.40 per 100,000 person-years in Brazil to as high as 2.5 per 100,000 person-years in regions like Curaçao and Bangladesh. The disease is less frequent in children (0.34 - 1.34 per 100,000 person-years) and becomes more prevalent with age[2].

In India, there is limited data on the population-level burden of GBS. Small case series indicate GBS as a significant cause of non-poliomyelitis acute flaccid paralysis (AFP), including fatal cases[3]. However, it remains uncertain whether axonal subtypes like AMAN are more common than AIDP, as observed in other developing nations[4].

Clinically, GBS patients often develop cranial nerve involvement, particularly facial or pharyngeal weakness. The characteristic ascending flaccid paralysis evolves over days to weeks. Autonomic dysfunction is common, manifesting as wide blood pressure fluctuations, postural hypotension, and cardiac arrhythmias. Approximately one-third of hospitalised patients require ventilatory support due to respiratory failure and oropharyngeal weakness, making early management critical. Immunologically, GBS involves endoneurial inflammation of spinal nerve roots and distal nerve segments[5].

Antecedent infections, such as upper respiratory tract infections, often precede GBS onset by 10 - 14 days[5].

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Identified triggers include *Campylobacter jejuni* gastroenteritis, cytomegalovirus, *Mycoplasma pneumoniae*, Epstein-Barr virus, and influenza[6]. Diagnosis is supported by cerebrospinal fluid (CSF) analysis and electrodiagnostic testing, although both may appear normal in the early stages. AIDP remains the most prevalent form, accounting for 70 - 90% of cases, with variants like AMAN, acute motor sensory axonal neuropathy (AMSAN), and MFS also observed. Seasonal variations, influenced by infection patterns have been reported, with peaks in summer in Asian countries[7].

Management of GBS involves therapeutic plasma exchange (TPE) and intravenous immunoglobulin (IVIg), both effective when initiated early[8,9]. IVIg is often preferred due to fewer complications but comes with higher costs. Supportive care, including physical therapy, plays an integral role in reducing complications such as respiratory issues, deep vein thrombosis, and delayed mobility[10].

Plasma exchange (PE), proven effective within four weeks of onset, typically involves four sessions (50 mL/kg/session) using fresh frozen plasma or albumin-saline mixtures. IVIg, administered at 0.4 g/kg/day for five days, shows comparable efficacy to PE when given within two weeks of symptom onset[9]. Given the socio-economic constraints of patients in India, particularly those from middle- and lower-income groups, the high cost of treatment poses a significant burden. Prolonged ventilatory support further increases the risk of complications like ventilator-associated pneumonia and sepsis, emphasizing the need for comprehensive ICU management[11].

This study aims to provide insights into the burden, management, and outcomes of GBS, addressing gaps in knowledge to improve clinical and public health strategies.

Material and Methods

Study Setting

The study was conducted at a tertiary care hospital in South Gujarat, affiliated with a government medical college.

Study Design

This was a retrospective, observational study.

Study Population

The study included all confirmed cases of Guillain-Barré Syndrome (GBS) admitted to the Department of General Medicine at the tertiary care hospital.

Inclusion Criteria

- Patients aged >18 years.
- All diagnosed cases of GBS admitted to the tertiary care hospital.

Exclusion Criteria

- Myopathies due to electrolyte imbalance.
- Paralysis resulting from vascular causes.

Sampling Technique

Convenience sampling was used.

Sample Size

The sample size was calculated using OpenEpi software with a 95% confidence interval and 80% power. Based on the mean ICU stay duration reported by Charra B *et al*[12], which was 38.2 ± 7.6 days for the IVIg group and 52.4 ± 5.3 days for the PE group, the minimum required sample size was determined to be 50 patients in each group.

Study Period

The study was conducted from July 2020 to February 2023.

Data Collection

Ethical clearance was obtained from the Institutional Ethics Committee (IEC) before initiating the study. Data were collected retrospectively from patient records using a predesigned proforma. Patients with neurological weakness were evaluated, and treatments with plasma exchange (PE) or intravenous immunoglobulin (IVIg) were assigned. Morbidity and therapeutic outcomes were assessed through clinical, cerebrospinal fluid (CSF), and electrophysiological evaluations. CSF analysis in 60 patients identified albumin-cytological dissociation, while electrophysiological studies distinguished neuropathic subtypes.

Diagnostic Criteria

The Brighton Diagnostic Criteria for Guillain-Barré Syndrome (GBS) was applied, including symmetrical flaccid weakness, decreased reflexes, monophasic onset (12 hours - 28 days), elevated CSF protein, supportive nerve conduction studies, and exclusion of alternative diagnoses.

Outcome Assessment

Patient outcomes were evaluated using the Hughes Disability Scale (0 - 6), ranging from normal function (0) to death (6).

Data Analysis

Data were entered into Microsoft Excel version 2023 (Microsoft Corporation, Redmond, Washington, United

States) and analysed using Epi Info 7.2 software. Descriptive statistics and inferential statistics were appropriately used to summarize the findings.

Ethical Considerations

Ethical clearance was obtained from the IEC, and the study was conducted in accordance with the ethical guidelines. Confidentiality was strictly maintained, and patient information was used solely for study purposes.

Results

The study included 100 participants with Guillain-Barré Syndrome (GBS)

Table I: Age and gender distribution of study participants (N = 100).

Variable	Participants Receiving IVIg Therapy (n=50)	Participants Receiving Palsma Exchange Therapy (n=50)	Total
Age (years)			
18 - 30	18 (36%)	14 (28%)	32
31 - 60	32 (64%)	36 (72%)	68
Mean ± SD	31.5 ± 4.1	36.0 ± 2.8	
Gender			
Male	32 (64%)	33 (66%)	65
Female	18 (36%)	17 (34%)	35

Table I presents the demographic distribution of the study participants. The cohort was divided into two treatment groups: intravenous immunoglobulin (IVIg) therapy (n = 50) and plasma exchange (PE) therapy (n = 50). In terms of age, most participants were aged 31 - 60 years, comprising 68% of the total population. The mean age for the IVIg group was 31.5 ± 4.1 years, while the PE group had a mean age of 36.0 ± 2.8 years. Regarding gender, males predominated in both groups, making up 64% in the IVIg group and 66% in the PE group, resulting in an overall male-to-female ratio of 65:35.

Table II: Clinical presentation, HIV status, and CSF analysis of study participants.

Category	Number	Percentage (%)
Clinical feature (N = 100)		
Acute onset flaccid paralysis	100	100
Hyporeflexia/Areflexia	100	100
Bilateral symmetrical or asymmetrical weakness	100	100
History of fever	50	50
Bowel and bladder involvement	0	0
History of trauma	0	0
Sensory involvement	10	10
History of unknown substance poisoning	2	2
Drug history	0	0
Precipitating event (GIT/Respiratory)	80	80
HIV status (N = 100)		
HIV Positive	10	10
HIV Negative	90	90
Cerebrospinal Fluid (CSF) Analysis (N = 60)		
Albumin-cytological dissociation	22	37
No albumin-cytological dissociation	38	63

Table II summarises the clinical features, HIV status, and cerebrospinal fluid (CSF) analysis of the participants. All 100 participants exhibited acute-onset flaccid paralysis, hyporeflexia/areflexia, and bilateral weakness. Fifty per cent of participants had a history of fever, and 80% experienced a precipitating event, such as gastrointestinal or respiratory infections. Sensory involvement was observed in 10%, while 2% had a history of unknown substance poisoning. No participants reported trauma or bowel/bladder involvement. HIV testing revealed 10% positivity, and CSF analysis performed in 60 participants showed albumin-cytological dissociation in 37%, while 63% lacked this finding.

Table III: Laboratory parameters and Nerve conduction velocity (NCV).

Laboratory Parameters (N = 60)			
Parameter	**Feature**	**Number**	**Percentage (%)**
WBC	Within normal range	17	28
	Leukocytosis	43	72
Serum Protein	Within normal range	49	82
	Hypoproteinaemia	11	18
Nerve Conduction Velocity (NCV) Findings (N = 100)			
Neuropathy Type		**Number**	**Percentage (%)**
Axonal Neuropathy		20	20
Demyelinating Neuropathy		68	68
Mixed Neuropathy		12	12

Table III provides an overview of laboratory parameters and nerve conduction velocity (NCV) findings in the participants. Among the 60 participants assessed, leukocytosis was observed in 72%, and hypoproteinaemia was seen in 18%. NCV findings revealed that 68% of participants had demyelinating neuropathy, 20% had axonal neuropathy, and 12% exhibited mixed neuropathy, indicating a diverse range of neuropathic patterns.

Table IV: Disability grade, mechanical ventilation, and hospitalisation.

Disability Grade (Mean ± SD)				
Time-point	**IVIg (n = 50)**	**Plasma Exchange (PE) (n = 50)**	**P-Value**	**95% CI**
At presentation	4.06 ± 0.11	4.2 ± 0.07	0.23	(-0.17 to -0.10)
Immediate post-therapy	3.27 ± 0.16	3.02 ± 0.09	0.06	(0.22 to 0.28)
After 4 weeks	2.29 ± 0.27	1.31 ± 0.16	0.001	(0.92 to 1.02)
Mechanical Ventilation Requirement (N=100)				
Ventilation Status	**IVIg (n = 50)**	**PE (n = 50)**		**P-Value**
Required	38 (76%)	32 (64%)		0.9
Not Required	12 (24%)	18 (36%)		
Hospitalisation Duration (Days)				
Duration	**IVIg (n = 50)**	**PE (n = 50)**		**P-Value**
1–30 days	13	21		0.22
31–60 days	29	24		
>60 days	8	5		
Weaning from Mechanical Ventilation (Days)				
Treatment	**Mean ± SD**		**P-Value**	**95% CI**
IVIg	37.7 ± 5.8		0.04	(-19.7 to -17.4)
PE	19.1 ± 3.5			

Table IV outlines the disability grade, mechanical ventilation requirements, and hospitalisation duration across the two treatment groups. Disability grades at presentation showed no significant difference between the groups (p = 0.23). However, significant improvement was observed at four weeks post-treatment, with the PE group showing a lower disability grade (mean of 1.31 ± 0.16) compared to the IVIg group (mean of 2.29 ± 0.27, p = 0.001). Mechanical ventilation was required for 76% of IVIg patients and 64% of PE patients, with a significantly shorter weaning duration for the PE group (mean of 19.1 ± 3.5 days versus 37.7 ± 5.8 days for IVIg, p = 0.04). Hospitalisation duration was similar between the two groups (p = 0.22).

Table V: Treatment outcome and mortality.

Outcome of Treatment (N = 100)				
Outcome	**IVIg (n=50)**	**PE (n = 50)**	**P-Value**	
Death	16 (32%)	4 (8%)	0.003	
Treated	34 (68%)	46 (92%)		
Comparative Analysis of Disability Grades				
Timepoint	**IVIg (n = 50)**	**PE (n = 50)**	**P-Value**	**95% CI**
At presentation	4.06 ± 0.11	4.2 ± 0.07	0.23	(-0.17 to -0.10)
Immediate post-therapy	3.27 ± 0.16	3.02 ± 0.09	0.06	(0.22 to 0.28)
After 4 weeks	2.29 ± 0.27	1.31 ± 0.16	0.001	(0.92 to 1.02)

Table V presents the treatment outcomes and mortality rates between the two groups. The mortality rate in the IVIg group was significantly higher (32%) compared to the PE group (8%, p = 0.003). The PE group also had a higher proportion of patients treated successfully (92%) compared to the IVIg group (68%). Additionally, disability grades at different time points indicated a more favourable outcome in the PE group, with significantly lower disability scores at four weeks post-treatment (p = 0.001).

Discussion

This retrospective study analysed 100 confirmed cases of Guillain-Barré Syndrome (GBS) admitted to a tertiary care hospital in South Gujarat, India, from July 2020 to February 2023. The primary objective was to evaluate the therapeutic effects of plasma exchange (PE) and intravenous immunoglobulin (IVIg) in treating GBS. Fifty participants were treated with IVIg and the remaining 50 with PE.

Age Distribution

The mean age of participants in the IVIg group was 31.5 years, and for the PE group, it was 36 years. This difference was not statistically significant. These findings align with studies conducted by Charra *et al*[12], where the mean ages for IVIg and PE groups were 37.4 and 30.7 years.

Gender Ratio

The male-to-female ratio in this study was 1:0.6 in the IVIg group and 1:0.5 in the PE group. These ratios are consistent with findings reported by Sonawale *et al*[11] and Kishore *et al*[13], which reported male-to-female ratios of 1:0.6 for both treatment modalities.

Clinical Presentation

All participants in both groups exhibited acute onset flaccid paralysis, hyporeflexia/areflexia, and bilateral symmetric weakness. Sensory involvement was noted in 10% of cases. Precipitating events, predominantly gastrointestinal and respiratory infections, were reported in 80% of cases. These findings are similar to those of Charra *et al*[12], who observed flaccid paralysis, hyporeflexia/areflexia, and bilateral symmetric weakness in all patients, with sensory involvement in 46% and gastrointestinal or respiratory infections in 51.2%.

Cerebrospinal Fluid Analysis

Albuminocytological dissociation was observed in 37% of participants in this study, compared to 85% reported by Sonawale *et al*[11]. Hypoproteinaemia and leukocytosis were noted in 34% and 63% of participants, respectively.

Disability Grade Improvement

The mean disability grade at presentation was 4.06 in the IVIg group and 4.2 in the PE group, with no statistically significant difference. However, after 4 weeks of therapy, the mean disability grade improved significantly in both groups, with values of 2.29 for IVIg and 1.31 for PE. This indicates that while both treatments are effective, PE showed marginally superior results. These findings are consistent with Kishore *et al*[13] and Leonhard *et al*[14], who reported similar trends in disability grade improvement.

Nerve Conduction Studies

In this study, demyelinating neuropathy was the most common finding on nerve conduction velocity (NCV) studies, observed in 68% of participants, followed by axonal neuropathy (20%) and mixed neuropathy (12%). These findings align with the studies by Rath *et al*[15].

Duration of Mechanical Ventilation Weaning

The mean duration of weaning off mechanical ventilation was significantly longer in the IVIg group (37.7 days) compared to the PE group (19.1 days). This result is similar to the findings of previously done study results by Elahi *et al*[16].

Outcome and Mortality

The mortality rate in this study was significantly higher in the IVIg group (32%) compared to the PE group (8%). This difference is consistent with findings from El-Bayoumi *et al*[17], which reported mortality rates of 18.7% and 14.2% for IVIg and PE groups, respectively, in mechanically ventilated children with GBS.

Limitations

This study being a retrospective study, it relies on previously recorded data, which may introduce information bias and limit the scope of analysis. Additionally, the sample size is relatively small, emphasizing the need for future multicentric studies with larger cohorts to improve generalisability.

Conclusion

The findings of this study reinforce the effectiveness of both IVIg and PE in managing GBS, with PE showing marginally better outcomes in terms of disability grade improvement, shorter mechanical ventilation duration, and lower mortality rates. These results contribute to the growing body of evidence supporting the use of plasma exchange as a preferred therapeutic modality in certain cases of GBS.

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Neutrophil-to-Lymphocyte Ratio as a Prognostic Marker in Alcoholic Liver Cirrhosis Complicated by Hepatic Encephalopathy: A Prospective Observational Study from North India

Ambadas Rathod, Pritam Singh**, Kamal Singh**, Anshu Palta***, Parth Sharma**

Abstract

***Background:** The neutrophil-to-lymphocyte ratio (NLR) reflects systemic inflammation in cirrhosis, but its prognostic role in Indian patients with alcoholic cirrhosis (ALC) and hepatic encephalopathy (HE) remains unclear. We compared NLR with Model for End-stage Liver Disease (MELD) and Discriminant Function (DF) scores for predicting 90-day mortality.*

***Methods:** This prospective cohort study enrolled 60 male patients with ALC and HE at GMCH, Chandigarh between July 2023 and January 2025. NLR, MELD, and DF scores were calculated at the time of admission. Outcomes were tracked for 90 days. ROC analysis and Cox regression were used to assess predictive performance.*

***Results:** Mean NLR was comparable between survivors (9.7 ± 11.3) and non-survivors (10.1 ± 7.3; p = 0.885). All markers showed poor discrimination (AUC: NLR = 0.587, MELD = 0.633, DF = 0.626; p >0.05). Sensitivity was high (NLR: 95.5%; MELD: 100%), but specificity was low (13.2 - 15.8%). Negative Predictive Value (NPV) was robust (NLR: 85.7%; MELD: 100%), suggesting utility in ruling out mortality.*

***Conclusion:** NLR did not significantly predict mortality but demonstrated high NPV, supporting its role in risk stratification. MELD/DF scores also lacked precision, underscoring the need for more accurate prognostic tools in ALC with HE.*

Introduction

Alcoholic Liver Disease (ALD) is a common global health issue that comprises a wide spectrum of conditions ranging from mild hepatic steatosis to cirrhosis and hepatocellular carcinoma (HCC). Long-term consumption of alcohol initiates macrovesicular fatty changes, followed by hepatic necrosis. Finally, it reaches irreversible diffuse fibrosis, disrupting chronic liver disease (CLD), characterised by parenchymal distortion and regenerative nodules[1].

The primary cause of cirrhosis is alcohol in Indian adults (43.2%), followed by NAFLD (14.4%), Hepatitis B virus (HBV) (11.5%), and Hepatitis C virus (HCV) (6.2%). Viral hepatitis-related cirrhosis is declining, while alcohol and NAFLD-related cases are rising[2].

ALD contributes significantly to the worldwide illness burden and is one of the main reasons for hospitalisation. The Asia-Pacific area is responsible for 54.3% of all cirrhosis-related deaths, making cirrhosis the primary cause of liver-related mortality[1].

Liver cirrhosis is characterised by an early phase of compensation which has a better outcome, followed by an advanced phase of decompensation which is associated with complications such as upper GI bleeding, portal hypertension, and HE[3].

HE is a reversible neuropsychiatric condition linked to liver cirrhosis. As a major complication of cirrhosis, HE contributes to high mortality rates and imposes a substantial economic burden on healthcare systems[1,4]. Studies indicate that around 30 - 40% of cirrhosis patients develop HE as a result of impaired liver function and portosystemic shunting[4]. The condition manifests with prominent clinical symptoms, leading to a worsened prognosis and a marked deterioration in patients' quality-of-life[5]. Research has shown that overt hepatic encephalopathy carries a grim outlook, with one-year mortality rates reaching 64%, escalating to as high as 85% within three years[2,6].

The course of HE is related to systemic inflammation activation and immune disorders[3]. Immunodeficiency and systemic inflammation are concurrent variables that exacerbate liver cirrhosis. Inflammation is indicated by the increased production of pro-inflammatory cytokines and their increased blood levels[7]. The lymphocyte count is related to the regulatory immune pathway, whereas the neutrophil count provides information on ongoing inflammation. Raised NLR has been demonstrated to predict medium and long-term mortality in liver cirrhosis more recently[7]. NLR is a simple inflammatory marker derived from

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differential white blood cell count. It is linked to poor prognosis in several cancers, (e.g., colorectal, hepatocellular, and pancreatic) and cardiovascular conditions, including peripheral vascular disease, coronary artery ectasia, and hypertension[8].

Limited data is available in the literature on the usage of NLR as a prognostic marker in patients of ALC with HE, particularly in the context of the Indian population. Traditional scores such as MELD and Child Turcotte Pugh (CTP) did not include the inflammatory state of the patient. Hence, we conducted this study to predict the outcome of patients of alcoholic cirrhosis with HE by using NLR as a prognostic marker.

Material and Methods

Study population

A total of 60 patients diagnosed with alcoholic cirrhosis and hepatic encephalopathy were enrolled in this prospective cohort study, conducted at Government Medical College and Hospital, Sector 32, Chandigarh, India.

Inclusion criteria

- Age >18
- Patients diagnosed with alcoholic cirrhosis with hepatic encephalopathy (West Haven Criteria).
- Radiological imaging findings suggestive of Chronic Liver Disease (CLD) on USG.

Exclusion criteria

- Pregnant and breastfeeding female patients
- Malignancies such as HCC
- Other causes of Liver cirrhosis (viral hepatitis, autoimmune hepatitis, drug-induced liver disease).
- Other causes of altered mental status (uremic encephalopathy, CO2 narcosis, hypoglycaemia).

The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and was approved by the Ethical Review Committee of the GMCH Chandigarh.

Data Collection and Clinical Definitions

- Clinically relevant variables were collected from all enrolled patients, including patient characteristics, complications and laboratory data. Routine investigations (CBC, RFT, LFT, and Coagulogram) were sent for the patients who enrolled in the study. MELD and DF scores were calculated on the day of enrolment.
- NLR ratio is calculated by using differential WBC count for Neutrophils and Lymphocytes.
- The performance of the NLR ratio in predicting mortality was compared with the Discriminant Function score and MELD score at the end of 90 days.
- Alcoholic liver cirrhosis was diagnosed using clinical history, laboratory tests, and ultrasonographic findings.
- Hepatic encephalopathy was diagnosed following American Association for the Study of Liver Diseases (AASLD) guidelines and the West Haven Criteria (WHC). Affected patients exhibited notable personality shifts, erratic behaviour, dyspraxia, disorientation, lethargy, and confusion regarding time and space, with some progressing to coma.

Statistical analysis

Mortality in patients of alcoholic cirrhosis with hepatic encephalopathy from the day of admission till 90 days post-discharge was described using proportions, percentages, and distribution. Significance of differences between mean values of NLR, MELD score and Discriminant function were tested by using the Kolmogorov–Smirnov test or Mann–Whitney 'U' test. The chi-square test was employed to assess the significance of associations between clinical outcomes and independent variables. Sensitivity, specificity, area under the curve (AUC), positive predictive value (PPV), and negative predictive value (NPV) were calculated to evaluate the NLR in comparison to the MELD score and DF score. Data analysis was carried out using SPSS 26.0 software.

Observation and Results

Table I: Clinical features of patients with ALC and HE

Variable	Total (n = 60)	Survival group (n = 38)	Non-survival group (n = 22)	P*
Age (years)	47.6 ± 10.9	46.4 ± 10.4	49.8 ± 11.7	0.266
BMI (kg/m^2)	26.0 ± 1.9			
Diabetes	12 (20%)	6 (15.8%)	6 (27.3%)	0.284
Hypertension	15 (25%)	6 (15.8%)	9 (40.9%)	*0.030*
CAD	3 (5%)	0 (0%)	3 (13.6%)	*0.020*
CKD	4 (6.7%)	2 (5.3%)	2 (9.1%)	0.567
Alcohol consumption duration	19.6 ± 7.2	18.4 ± 6.4	21.7±8.2	0.113
Precipitating factors for HE				
SBP	16 (26.7%)	10 (26.3%)	6 (27.3%)	0.936
UGIB	21 (35%)	15 (39.5%)	6 (27.3%)	0.340
Infections other than SBP	9 (15%)	6 (15.8%)	3 (13.6%)	
Constipation	10 (16.7%)	4	6	0.131
Other causes	4 (6.6%)	1	3	0.099

HE		2 (1.3-2)	2 (1.8-3)	0.114
Grade 1	15 (25%)	10 (26.3%)	5 (22.7%)	
Grade 2	30 (50%)	21 (55.3%)	9 (40.9%)	
Grade 3	12 (20%)	5 (22.7%)	7 (18.4%)	
Grade 4	3 (5%)	0 (0%)	3 (13.6%)	
Hypotension on presentation		0 (0%)	4 (%)	0.007
HB (gm/dL)	8.5 ± 2.3	8.8 ± 2.1	8 ± 2.6	0.217
TLC (x10^3/µL)	13.3 ± 8.06	13.7 ± 8.9	12.7 ± 6.6	0.638
PLT (x10^3/µL)	110.2 ± 71.7	118.7 ± 66.4	97.4 ± 80.9	0.302
NLR	9.91± 9.99	9.7 ± 11.3	10.1± 7.3	0.885
Total Bil (mg/dL)	10.36 ± 11.70	8.7 ± 10.1	13.2 ± 13.8	0.217#
SGOT ((U/L)	240.73 ± 434.24	217.7 ± 479.2	280.6 ± 350.1	0.217#
SGPT ((U/L)	123.73 ± 328.93	140.8 ± 393	94.2 ± 174.5	0.939#
Albumin (g/dL)	2.33± 0.5	2.4± 0.5	2.3± 0.5	0.379
Creatinine (mg/dL)	1.93 ± 1.80	1.8 ± 1.9	2.1 ± 1.7	0.480#
Sodium (mEq/L)	133.58 ± 8.28	133.6 ± 8.3	133.5 ± 8.5	0.842#
PT (seconds)	21.85 ± 8.79	23.6 ± 12	20.8 ± 6.2	0.236
INR	1.71 ± 0.894	1.9 ± 1.2	1.6 ± 0.6	0.196
MELD Score	23.8 ± 8.7	22.3 ± 8.6	26.3 ± 8.6	0.87
DF score	44.7 ± 38.3	37.5 ± 24.9	57.2 ± 52.5	0.55

Patients were divided into two groups based on 90-day survival outcomes: survivors (n = 38) and non-survivors (n = 22). Their clinical characteristics are presented in Table I.

The survival group had a mean age of 46.4 ± 10.4 years, compared to 49.8 ± 11.7 years in the non-survival group. The most prevalent co-morbidities in the study population were hypertension (25%), diabetes mellitus (20%), followed by chronic kidney disease (6.7%) and coronary artery disease (5%).

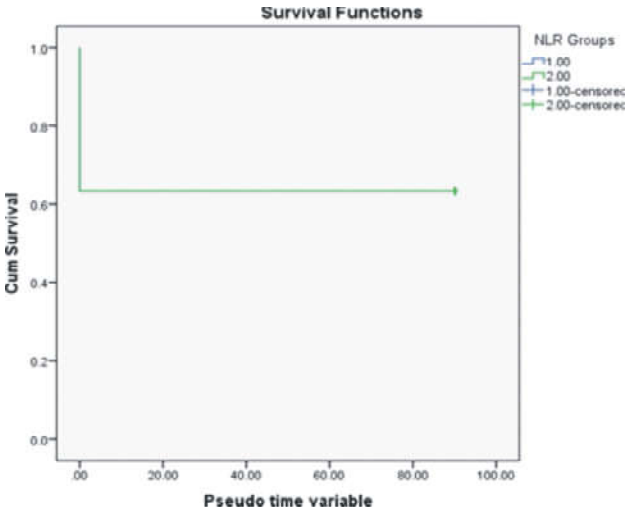

Fig. 1: *Kaplan-Meier survival analysis for 90-day mortality by NLR.*

The survival group had consumption of harmful alcohol for an average of 18.4 ± 6.4 years, while the non-survival group consumed it for an average of 21.7 ± 8.2 years.

The major precipitating factors for HE included: upper gastrointestinal bleeding (UGIB) (35%), spontaneous bacterial peritonitis (SBP) (26.7%), non-SBP infections (15%), constipation (16.7%) and other causes (6.6%). Regarding the severity of HE at presentation, grade 2 HE was the most common (50%), followed by grade 1 HE (25%), grade 3 HE (20%) and grade 4 HE (5%). The mean NLR showed no significant difference between groups (survivors: 9.7 ± 11.3 vs non-survivors: 10.1 ± 7.3; p = 0.885), despite being slightly elevated in non-survivors.

Patients were stratified by median NLR (≤7.38 vs >7.38; 30 each). Both groups had 11 deaths (63.3% 90-day survival). The Kaplan-Meier survival analysis (Fig. 1) found no statistically significant difference between groups (p >0.05), indicating that median-dichotomised NLR does not serve as a reliable prognostic marker for 90-day survival in this population.

Table II: Correlation between baseline NLR and 90-day mortality risk

NLR	Mortality at 90 days	Total	Chi-square value	p value
	Non-survivor	Survivor		
	N (%)	N (%)	N (%)	1.709 0.191
<2.59	1 (4.5)	6 (15.8)	7 (11.7)	
≥2.59	21 (95.5)	32 (84.2)	53 (88.3)	
Total	22 (100.0)	38 (100.0)	60 (100.0)	

The analysis examined the relationship between neutrophil-to-lymphocyte ratio (NLR) dichotomised at a cut-off of 2.59 and 90-day mortality. The association was evaluated using a Chi-square test ($\chi^2 = 1.709$, p = 0.191). While a trend towards increased 90-day mortality was observed in patients with NLR ≥2.59 (Table II), this difference did not reach statistical significance. Thus NLR dichotomised at this threshold does not demonstrate a significant association with 90-day mortality in our study population.

Table III: Cox proportional hazards regression analysis of 90-day mortality.

Predictor Variable	Hazard Ratio (HR)	p-value
Age (years)	1.03	0.126
MELD Score	1.03	0.331
DF Score	1.005	0.313
NLR	0.996	0.875

Table III shows a Cox proportional hazards regression model that was used to examine the relationship between baseline

factors and 90-day death rates. The analysis revealed the following trends, though none reached statistical significance:

- A one-year increase in age was found to increase the risk of death by 3% (HR = 1.03, p = 0.126).
- MELD Score: A one-unit increase in MELD score increased the risk of death by 3% (HR = 1.03, p = 0.331).
- A one-unit increase in the DF score led to a 0.5% increase in the risk of death (HR = 1.005, p = 0.313).
- A one-unit rise in NLR resulted in a 0.4% reduction in the risk of death (HR = 0.996, p = 0.875).

In this analysis, one of the analysed variables (age, MELD score, DF score, or NLR) showed statistically significant associations with 90-day mortality in this cohort. Further studies with larger cohorts may be needed to identify robust predictors of short-term survival in this population.

Fig. 2 shows poor mortality prediction by all markers: NLR (AUC = 0.587, p = 0.263), MELD (AUC = 0.633, p = 0.089), and DF scores (AUC = 0.626, p = 0.107), with none reaching statistical significance. All AUCs neared 0.5, indicating negligible discrimination between survivors and non-survivors. No variable demonstrated statistically significant predictive capability.

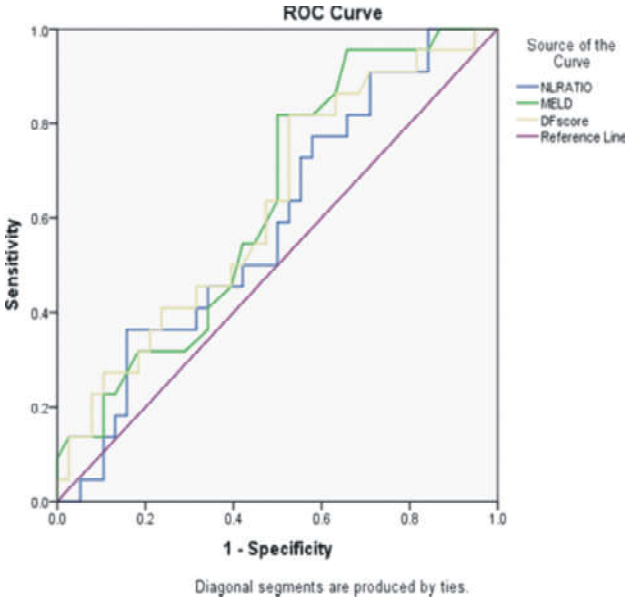

Fig. 2: *Assessment of 90-day mortality prediction using receiver operating characteristic (ROC) curves.*

Table IV: Comparison of predictive performance for 90-day mortality

Metric	NLR (Cut-off: 2.595)	MELD (Cut-off: 13)	DF Score (Cut-off: 10.85)
Sensitivity (%)	95.5	100	95.5
Specificity (%)	15.8	13.2	15.8
PPV (%)	39.6	40	39.6
NPV (%)	85.7	100	85.7

All three variables showed excellent sensitivity (MELD: 100%; NLR/DF: 95.5%) but poor specificity (MELD: 13.2%; NLR/DF: 15.8%) as shown in Table IV. While they effectively identified true positives (high sensitivity), false positives were common (low specificity). Positive predictive values were uniformly modest (~40%), indicating limited reliability for mortality prediction. However, negative predictive values were stronger (MELD: 100%; NLR/DF: 85.7%), suggesting better utility in ruling out mortality risk. The MELD score demonstrated perfect sensitivity and NPV, but all markers suffered from low specificity, limiting their clinical utility as standalone predictors. These patterns highlight a trade-off between sensitivity and specificity in mortality prediction.

Discussion

Alcoholic cirrhosis complicated by hepatic encephalopathy presents a significant clinical challenge, marked by high morbidity and mortality. Accurate prognostication in these patients is essential for optimizing clinical management and resource allocation. This study aimed to assess the prognostic value of the neutrophil-to-lymphocyte ratio (NLR) in predicting 90-day mortality among patients with alcoholic cirrhosis and HE, thereby addressing the utility of NLR as a potential risk stratification tool.

Systemic inflammation, as reflected by NLR, has emerged as a mortality predictor in various liver diseases. Contemporary research has established a significant association between elevated NLR and adverse outcomes in advanced liver disease. Specifically, Shi *et al* demonstrated its prognostic value in overt hepatic encephalopathy[9], while Liu *et al* validated its mortality prediction in decompensated cirrhosis[10]. These findings collectively highlight the clinical utility of inflammatory biomarkers for risk stratification in this high-risk patient population.

In addition to evaluating NLR's prognostic value, this study also aimed to compare its predictive performance against established clinical scoring systems (MELD and DF scores) for 90-day mortality. The MELD score, as evident by studies like Bohra *et al* has been routinely employed in clinical practice to evaluate disease progression and predicts

mortality risk in patients with cirrhosis[11].

In our cohort, although higher NLR values were observed in non-survivors compared to survivors, this difference did not achieve statistical significance (p = 0.885). The mean age of participants was 47.6 ± 10.9 years, consistent with the age range typically reported for alcoholic liver disease, which often presents in the fourth to fifth decades of life. Compared to our findings, Sahani *et al* reported a higher mean age (62.2 years), while Bohra *et al* reported a mean age of 57 years[11,12]. This relatively younger cohort may reflect regional variations in alcohol use patterns or earlier disease onset.

The predominant proportion of our study cohort (70%) had a BMI of 25.0 kg/m^2 or greater, indicating a high prevalence of overweight or obesity. The mean BMI of our study population was 26.0 ± 1.9 kg/m^2. In the study conducted by Berzigotti *et al*[13], the mean BMI was 27.9 ± 4.8 kg/m^2. Obesity can exacerbate liver inflammation and fibrosis, potentially influencing the severity of hepatic encephalopathy and overall prognosis[14].

In our study, all enrolled patients were male. This contrasts with the study conducted by Liu *et al* where 72.9% of the participants were male and 27.1% were female[10]. These findings highlight that alcoholic cirrhosis is more prevalent among males compared to females, likely due to higher rates of alcohol consumption among men in Indian society.

Our cohort demonstrated substantial co-morbidity burden, with hypertension predominating (25%), followed by diabetes mellitus (20%), while CAD (5%) and CKD (6.7%) were less prevalent. These findings align with Mukthinuthalapati *et al* reported atherosclerotic disease (89.7%), diabetes (27.4%), CKD (8.5%), and HF (9.1%) in similar patients[15].

Regarding alcohol exposure, survivors reported significantly shorter duration of consumption (18.4 ± 6.4 years) compared to non-survivors (21.7 ± 8.2 years, p = 0.113). Grade 2 HE was most frequent (30 patients: 21 survival, 9 non-survival), followed by Grade 1 (15: 10 survival, 5 non-survival), Grade 3 (12: 5 survival, 7 non-survival), and Grade 4 (3: all non-survival). Higher HE grades correlated with increased mortality. These findings differ from the study conducted by Shi *et al* which reported 68.2% of patients with Grade 2 HE, 25.1% with Grade 3 HE, and 6.6% with Grade 4 HE[9]. Similarly, Bajaj *et al*[16] noted that patients presenting with grade 3 - 4 hepatic encephalopathy demonstrated significantly increased 30-day mortality rates, reinforcing the prognostic significance of HE.

Notably, the mean NLR was 9.91 ± 9.9, with a wide range from 1.50 to 54.60. The mean NLR in the survival group was 9.77 and 10.16 in the non-survival group. These findings indicate significant haematological abnormalities in our cohort. Rice *et al*[17] also analysed haematological parameters, showing an increased risk of mortality with a rising NLR up to 8. Patients were divided into two groups using the median NLR (≤7.38 vs >7.38), with 30 patients in each. Over 90 days, 11 deaths occurred in both groups, yielding identical cumulative survival rates of 63.3%. Kaplan-Meier survival analysis revealed no statistically significant difference in 90-day mortality between NLR-stratified groups. These results suggest that NLR, when dichotomised at the median, does not predict short-term mortality in this cohort. This contradicts the findings of a study that suggested that NLR >4 was associated with a greater risk of 90-day mortality[18].

The analysis of serum electrolytes and renal function parameters showed a mean serum sodium level of 133.5 ± 8.5 mEq/L in the non-survival group and 133.6 ± 8.2 mEq/L in the survival group. This is inconsistent with a study where the mean sodium in the survival group was 136 mEq/L as compared to 132 mEq/L in the non-survival group[19].

The survival group had a slightly lower mean MELD score (22.3 ± 8.6) than the non-survival group (26.3 ± 8.6). This is in contrast to Mallik *et al's* findings, which showed that the median MELD score was 21.03 in the non-survival group and 10.36 in the survival group[20]. These findings align with Bohra *et al* who reported a median MELD score of 25, consistent with advanced liver disease in their study[11].

In our study, the non-survival group had a notably higher mean DF score (57.2 ± 52.5) than the survival group (37.5 ± 24.9). This is in contrast to Monsanto *et al's* findings, in which the mean DF score was 48 in the survival group and 96 in the deceased group[21].

The analysis revealed non-significant statistical correlation between dichotomised baseline NLR at a cut-off value of 2.59 and 90-day mortality. The NLR was less than 2.59 in 15.8% of survivors and 4.5% of non-survivors. Whereas, it was greather than 2.59 in 84.2% of the survivors and 95.5% of the non-survivors. The data suggests a trend where a larger proportion of patients with NLR ≥2.59 died after 90 days compared to those with NLR <2.59, although the difference is not statistically significant (p = 0.191). In contrast to Biyik *et al* results showing markedly worse survival for NLR ≥2.72 (p <0.001) and consistent independent mortality prediction (OR 1.2, 95% CI, 1.2 - 1.3), our analysis failed to replicate these significant associations at similar NLR thresholds[22]. Therefore, while the observed frequencies suggest a possible relationship, there is not enough evidence to conclude a statistically significant association between NLR (using this cut-off) and 90-day mortality.

In our study ROC curve analysis yielded optimal cut-off values of 2.59 for NLR, 13 for MELD, and 10.85 for DF scores.

However, these thresholds demonstrated inadequate discriminatory power for 90-day mortality prediction (all AUCs <0.65, p >0.05), potentially reflecting the study's limited sample size, population heterogeneity (variations in co-morbidities, age, and disease severity), or the dynamic nature of cirrhosis-related complications.

The MELD score demonstrated 100% sensitivity but very low specificity (13.2%), while NLR and DF scores each showed high sensitivity (95.5%) but similarly low specificity (15.8%). The positive predictive values (PPV) for all three markers were modest (~40%), suggesting limited reliability in confirming mortality risk. In contrast, the negative predictive values (NPV) were relatively high 100% for MELD and 85.7% for NLR and DF, indicating that negative results were more reliable in predicting survival.

These findings differ from prior studies. Mallik *et al* reported MELD sensitivity, specificity, PPV, and NPV of 55.38%, 93.33%, 87.8%, and 70.7%, respectively[20]. Similarly, Maccali *et al* found that at an NLR cut-off of 3.6, sensitivity was 69%, specificity was 65%, PPV was 38%, and NPV was 87% for 90-day mortality prediction[6]. While our results align with previous studies in terms of sensitivity and NPV, all three scores exhibited poor specificity and PPV, limiting their utility as standalone prognostic tools.

Conclusion

This study reveals that while the neutrophil-to-lymphocyte ratio (NLR) lacks significant predictive power for mortality in alcoholic cirrhosis patients with hepatic encephalopathy, its exceptionally high negative predictive value (85.7%) offers crucial clinical utility by reliably identifying low-risk patients who may not require intensive intervention. Although traditional scores (MELD/DF) similarly showed limited prognostic accuracy, NLR's strength in ruling out mortality risk provides a simple, cost-effective tool for risk stratification in resource-limited settings. These findings highlight both the challenges in prognostication for this high-mortality population and the potential for NLR to optimise clinical decision-making, while underscoring the urgent need for more robust predictive models through future multicenter validation studies.

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REVIEW ARTICLE

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High Altitude Hypertension

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Abstract

***Background:** High altitude (HA) presents unique physiological challenges, primarily due to hypobaric hypoxia, which affects multiple organ systems, including the cardiovascular system. Blood pressure (BP) responses at HA vary widely, with some individuals experiencing transient or sustained hypertension. Understanding these responses is essential for optimizing medical management in individuals traveling to or residing at HA.*

***Objective:** This review examines the effects of HA on BP regulation, the physiological mechanisms underlying BP changes, the impact on normotensive and hypertensive individuals, and the role of antihypertensive medications in HA environments.*

***Findings:** Acute exposure to HA generally leads to an initial increase in BP, driven by sympathetic activation and vascular changes. While some individuals experience normalisation with acclimatisation, others develop persistent hypertension, which may indicate maladaptive responses. The prevalence of acute HA illnesses does not appear to be significantly different between normotensive and hypertensive individuals, though long-term cardiovascular risks remain uncertain. Medication selection for BP control at HA requires careful consideration, as some antihypertensive agents, such as ACE-inhibitors and beta-blockers, may have unintended effects on oxygenation and acclimatisation.*

***Conclusion:** BP regulation at HA is highly variable and influenced by individual adaptation. While most cases of HA hypertension are transient, persistent elevations warrant medical attention. Future research should explore the long-term cardiovascular consequences of HA exposure and refine treatment strategies for individuals with pre-existing hypertension. A proactive approach, including pre-travel assessment, continuous BP monitoring, and tailored medication adjustments, is essential for ensuring cardiovascular health at HA.*

Introduction

Enjoyment, work, and athletic competition draw a large number of people to high altitude. The key changes at high altitude (HA) include decreases in temperature and ambient humidity, but the defining environmental feature is a drop in barometric pressure, causing a decrease in the partial pressure of oxygen in the tissues. A series of physiological responses are triggered by this hypobaric hypoxia which, in most cases, help the individual tolerate and adapt to the low oxygen conditions. However, in other cases, maladaptive responses occur, leading to one of three forms of acute altitude illness: acute mountain sickness (AMS), high-altitude cerebral edema (HACE), and high-altitude pulmonary edema (HAPE).

Apart from these, hypertension is the most common cardiovascular disease observed in people sojourning at high altitudes[1,2]. The effect of chronic hypobaric hypoxia, induced by living at high altitude (HA), on blood pressure (BP) is uncertain and may vary across different populations. Research on this relationship and other cardiopulmonary changes at HA has been ongoing for more than 50 years[3], yet it remains uncertain whether the relationship between BP and HA is causal or a result of coincident lifestyle factors.

An inverse association between altitude and BP has been observed, which may be due to various factors. These include structural changes in the vasculature, as well as a number of socio-cultural, biological, chemical, and physical factors acting separately or in combination[4,5]. However, the possible benefit of altitude-related hypoxia on systemic BP may diminish when genetic and lifestyle-related risk factors become dominant, as seen in populations of Tibetan origin, where they start showing a hypertensive response[6,7].

Physiological Response to High Altitude

Acute exposure to high altitude (HA) leads to a decrease in blood pressure (BP) due to a reduction in systemic vascular resistance. Functional sympatholysis has been proposed as the probable explanation for this phenomenon. The indirect effect of hypobaric hypoxia at HA, acting via increased sympathetic activation, leads to vasoconstriction, whereas the direct effect of hypoxia on blood vessels causes vasodilation. This creates a conflict between two opposite effects on the blood vessels.

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Studies have shown that during acute exposure to HA, the direct effect of hypoxia dominates, causing vasodilation, a phenomenon known as functional sympatholysis. Over time, as acclimatisation occurs and the oxygen content of the blood increases, causing a reduction in cardiac output and stroke volume, functional sympatholysis diminishes. Hence, the indirect effect of hypoxia via sympathetic vasoconstriction leads to increased BP during chronic exposure[8].

Thus, acute hypoxia initially causes a decrease in BP, followed by an increase, which continues until the acclimatisation process mitigates hypoxia, leading to a subsequent BP reduction or near-normalisation. However, in the Indian population, this initial BP decrease has not been observed; rather, acute exposure raises BP, followed by a decline with long-term exposure. A similar initial BP increase has been noted in white lowlanders during the early days of acute HA exposure[9-11].

Several explanations for this BP response have been proposed, including adrenergic system activation, increased arterial stiffness, endothelin (ET) release, and reduced vasodilatory responses[12,13]. This BP increase generally lasts for about 6 days (the acclimatisation period) but can persist for up to 9 weeks.[14] Conversely, long-term exposure to HA (more than 2 years) in white lowlanders has been associated with a reduction in both systolic and diastolic BP[15]. This is supported by evidence showing that HA natives exhibit a lower prevalence of hypertension[16].

Behaviour of Normotensives and Hypertensives at High Altitude

The effect of HA on BP in normotensive individuals has shown varied responses. Normotensive individuals may experience an increase, decrease, or no change in BP during acute exposure to HA[17-19]. On the other hand, hypertensive individuals have shown either a BP increase of up to 15 mm Hg or no significant change upon acute exposure[20,21].

In hypertensive individuals at rest, an initial BP increase is observed, followed by a gradual decline over days to weeks[20-22]. During exercise, a slightly greater BP increase has been noted in hypertensives compared to normotensives[21]. Thus, while both groups exhibit variable BP responses at HA, hypertensives tend to experience a more pronounced BP rise than normotensives.

Origin of Hypertension at High Altitude in Normotensives

A study found that after residing at HA for 12 months, more than 60% of initially normotensive individuals had systolic blood pressure (SBP) higher than optimal levels, while others maintained SBP within the normal range. Among them, 40% were actually hypertensive [diastolic blood pressure (DBP) >90 mmHg][23]. This indicates that, regardless of the duration of hypoxia exposure and the normalisation of oxygen content, some healthy individuals develop elevated systemic arterial pressure[24].

Normotensive individuals at sea level who ascend to HA frequently experience hypertension, as evidenced by abnormal 24-hour ambulatory systolic and diastolic BP values, along with increased daytime and nighttime BP readings[25]. Several factors have been proposed for hypertension at HA, including persistent sympathetic stimulation[26], an enhanced chemoreceptor reflex (noted in individuals prone to hypertension)[27], and the presence of "hyper-responders", who are predisposed to developing high-altitude pulmonary hypertension, along with a general lack of tolerance[28]. BP in individuals ascending to HA often remains elevated even after acclimatisation, primarily due to two key factors: they may be delayed acclimatisers, or they were borderline hypertensive at sea level, with their condition becoming apparent under the physiological stress of HA.

Our Research

A total of 600 patients with raised BP were analysed at a hospital located at HA to establish the relationship between hypertension and the duration of stay at HA. Hypertension was seen in the majority of individuals in the early days of arrival at HA, while the rest developed it over a period of two years at different times. Upon further investigation, it was discovered that most hypertensive patients at HA were affected within the first 3 months of their stay. Further analysis revealed that, among these cases, the majority developed hypertension within the first week of arrival. Hence, it was hypothesised that impaired acclimatisation might be contributing to hypertension.

To explore this further, we conducted a detailed study examining BP trends in individuals traveling to HA during the first 6 days of the acclimatisation period. A total of 398 normotensive sojourners from sea level ascending to HA (3,500 m) were studied, and their BP responses were recorded for six consecutive days at HA. Based on their BP response on the 6th day, they were divided into two groups: HBP (high BP group) and NBP (normal BP group).

Upon analysing the results, it was found that on the 6th day at HA, 347 out of 398 individuals normalised their BP (BP 140/90 mmHg. A detailed analysis of BP trends showed that the NBP group initially exhibited raised BP, which returned to normal levels within the 6-day acclimatisation period. However, in the HBP group, BP continued to rise from the 4th day onward.

Hence, it can be concluded that individuals whose BP does not return to normal by the 6th day at HA require regular follow-up, as they may experience delayed acclimatization leading to later BP normalisation or may develop persistent hypertension[29].

Consequences of High BP at High Altitude

The first question to address was whether the prevalence of acute HA illnesses is higher in hypertensive individuals than in normotensive individuals. According to the literature, one study found that the prevalence of acute mountain sickness (AMS) is not different between normotensive and hypertensive travelers[3].

Regarding high-altitude pulmonary oedema (HAPE), increased susceptibility in hypertensive individuals has never been formally investigated. Furthermore, there is no existing data linking hypertension to an increased risk of high-altitude cerebral oedema (HACE).

Additionally, we examined whether the complications of hypertension are more prevalent in hypertensive individuals compared to normotensive individuals at high altitude. Observations revealed that, in resting conditions, complications such as hypertensive retinopathy, intracranial bleeding, or myocardial infarction were not reported, even when systolic blood pressure (SBP) exceeded 190 mmHg or diastolic blood pressure (DBP) surpassed 125 mmHg for up to 28 to 42 days at high altitude[20]. Similarly, no complications were reported during exercise in individuals with hypertension at HA[31].

Many cases of sudden cardiac death (SCD) have been documented at high altitude[32], but a higher incidence of SCD in individuals with a prior history of hypertension has been associated with physical activity at HA. However, confounding variables such as fasting, hydration, physical fitness, and mountain activities were not accounted for[33]. Although hypertension has been observed in cases of SCD at HA, no study has established a direct causal link[34].

In conclusion, the majority of studies have dismissed the risk of complications arising in hypertensive individuals at high altitude. However, further research is needed.

Medication Selection for Blood Pressure Control at High Altitude

Studies have shown that angiotensin-converting enzyme (ACE) inhibitors increase the hypoxic ventilatory response and improve high-altitude tolerance, making them a viable option for managing hypertension at HA[35]. However, ACE inhibitors have also been found to impair renal erythropoietin production, which could negatively impact haematologic responses at high altitude[36]. Therefore, their overall utility at altitude remains uncertain.

Angiotensin receptor blockers (ARBs), such as Telmisartan, have been shown to reduce both daytime and nighttime BP, but this effect has only been observed up to an altitude of 3,400 m. At 5,400 m, the drug was found to be ineffective due to the concomitant suppression of the renin–angiotensin system[25]. A combination of an ARB and a calcium channel blocker has been proven effective and safe in reducing BP in both untreated and previously treated hypertensive patients[3].

Beta-blockers have also been studied for hypertension at high altitude. Non-selective betablockers, such as Carvedilol, used in healthy individuals, have led to a significant reduction in BP at HA but were associated with decreased oxygen, saturation and reduced exercise tolerance. However, these side-effects have not been observed with highly selective beta-1 blockers like Nebivolol. Nebivolol effectively reduces BP at HA while preserving normal nocturnal BP dipping and causing less reduction in exercise tolerance[38].

Another highly useful drug is acetazolamide, which is commonly used to treat high-altitude illnesses. It has been found to help reduce BP elevation while also improving sleep apnea[39].

Important Observations from these Studies

The following key observations have been made across various studies on hypertension at high altitude:-

1. A large degree of interindividual variability in blood pressure responses at HA.
2. Inability to predict who will exhibit a brisk or blunted blood pressure response at high altitude.
3. Most studies have been conducted at elevations below 3,500 m, making it difficult to draw conclusions about blood pressure responses in hypertensive patients at elevations above 3,500 m.
4. Ethnic differences in blood pressure responses at HA have not been evaluated.
5. Studies primarily included individuals with mild-to-moderate hypertension, resulting in limited information about those with severe or highly variable (labile) hypertension.

Recommendations: Advice for Individuals Traveling to High Altitude

1. For individuals with uncontrolled hypertension planning to ascend to HA, the following is recommended:

Pre-exposure ambulatory BP monitoring should be conducted before induction to HA.

Ascent is absolutely contraindicated if:

a) Resting BP exceeds 160/100 mmHg, or

b) Systolic BP exceeds 220 mmHg during exertion

2. Medication adjustments for hypertensive individuals at HA should be made in two situations:

   a) If SBP >180 mmHg or DBP >120 mmHg, along with symptoms such as vision changes, shortness of breath, chest pain, or altered mental status.

   b) If SBP >220 mmHg or DBP >140 mmHg, even in the absence of symptoms.

   c) Transient BP elevations lasting only a few minutes should not prompt medication adjustments. Adequate rest should be ensured before measuring BP.

3. At HA, medication adjustments should be considered if hypertensive individuals show increased BP. However, since BP may decrease with acclimatisation, the following approach is recommended:

   a) Continuous BP monitoring to prevent excessive BP reduction or symptoms of hypotension.

   b) Upon descent to lower elevations, medications should be reverted to their original regimen.

4. For individuals with mild to moderate hypertension:

   a) If BP elevation is noted at HA, antihypertensive doses should not be increased immediately; instead, monitoring is recommended.

   b) For individuals with poorly controlled, labile hypertension or those with a history of marked BP increases at HA. BP should be closely monitored.

   c) If BP remains elevated, increase the dose of antihypertensive medication.

   d) If BP remains elevated despite dose adjustments, a second antihypertensive should be added.

   e) Throughout treatment, it is crucial to ensure that individuals do not experience symptoms of hypotension or syncope.

Conclusion

The initial increase in BP is a necessary adaptation to maintain oxygen supply to cells in a hypoxic environment. However, a sustained rise in BP indicates improper acclimatisation, where the body compensates by increasing BP instead of utilizing other physiological mechanisms.

BP responses at high altitude are highly unpredictable, affecting both normotensive and hypertensive individuals. A normotensive individual may develop persistent hypertension at HA, while a hypertensive may experience normalisation of BP.

There is no strong evidence in the literature suggesting increased mortality among hypertensive individuals at HA, except for a few anecdotal reports. Hypertension at HA differs from hypertension at sea level as it is initially a form of secondary hypertension, and target organ damage is difficult to assess since BP remains elevated throughout HA exposure.

The most effective drugs for managing hypertension at HA include ACE inhibitors, Angiotensin Receptor Blockers (ARBs), and Calcium Channel Blockers. However, caution is necessary – individuals taking antihypertensive medications must be informed to monitor their BP upon returning to lower altitudes and adjust their medication under medical supervision to prevent hypotension and syncope.

Ultimately, early recognition and management of HA hypertension are crucial to preventing long-term elevated BP at high altitude.

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CASE SERIES

JIACM 2025; 26 (3): 137-39

Right Atrial Thrombosis with Inferior Vena Cava Extension in Chronic Obstructive Pulmonary Disease: A Case Series

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Abstract

Background: Right atrial (RA) thrombosis, particularly in association with inferior vena cava (IVC) thrombosis, is rare and potentially fatal. Known causes include cardiac interventions, malignancies, and congenital anomalies. However, data on conservative management of idiopathic RA thrombosis, especially in the setting of chronic obstructive pulmonary disease (COPD), is limited.

Aim: To describe the clinical presentation, management, and outcomes of three patients with RA and IVC thrombus without conventional thrombotic risk factors.

Methods: This case series includes three male smokers with underlying COPD presenting with acute breathlessness. 2D echocardiography revealed thrombi extending from the IVC into the RA. Routine blood parameters were normal, and thrombophilia screening was negative.

Results: All patients were managed conservatively with intravenous heparin followed by oral anticoagulation. Serial echocardiograms showed complete thrombus resolution within 14 to 31 days. No complications or embolic events were recorded. COPD management was optimised.

Conclusion: COPD may act as a prothrombotic milieu leading to RA and IVC thrombosis in the absence of classical risk factors. Conservative anticoagulation therapy can result in complete resolution. Larger studies are needed to further explore this association and optimise treatment strategies.

Key words: Right atrial thrombus, inferior vena cava, COPD, anticoagulation.

Introduction

Virchow's triad describes the three principal mechanisms for thrombus formation: endothelial injury, stasis of blood flow, and hypercoagulable state. Right atrial thrombosis is a rare and serious clinical condition, particularly when associated with inferior vena cava (IVC) thrombus, due to the risk of pulmonary embolism. Documented causes include heart failure, congenital heart disease, invasive interventions, malignancies, and thrombophilic disorders. However, right atrial thrombus without these aetiologies is uncommon. This case series highlights three such instances in male patients with chronic obstructive pulmonary disease (COPD) and a history of smoking, with no other identifiable risk factors.

Case Reports

Case 1

A 56-year-old male with a 30-pack-year smoking history and GOLD Stage 3 COPD presented with MMRC Grade 4 dyspnoea. Initial chest radiograph showed pulmonary oedema. 2D echocardiography revealed a thrombus in the IVC extending into the RA, with diastolic dysfunction and pulmonary hypertension. Thrombophilia work-up, including Protein C and S, was negative. The patient was treated with intravenous heparin (5,000 IU QID) for 7 days, followed by oral dabigatran from day 5. COPD was managed concurrently. Follow-up echo on day 15 showed complete thrombus resolution.

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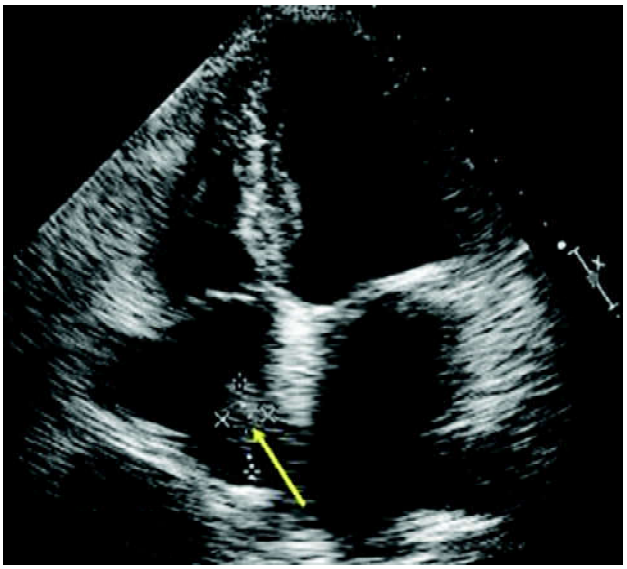

Fig. 1: *Showing thrombus in the right atrium.*

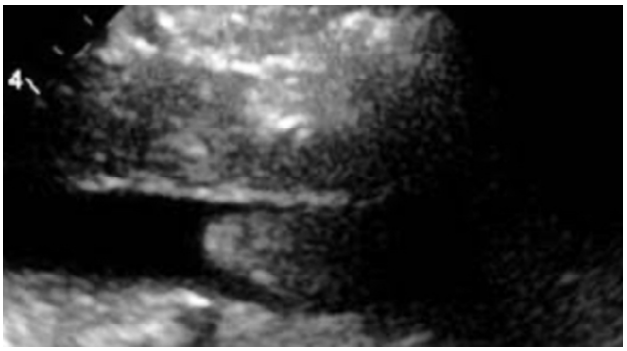

Fig. 2: *Showing IVC thrombus.*

Case 2

A 60-year-old male smoker with GOLD stage 3 COPD presented with MMRC Grade 3 dyspnoea and signs of right heart failure. 2D echo revealed an IVC thrombus extending into the RA. Lab investigations were unremarkable. The patient received intravenous heparin for 7 days, bridged to oral anticoagulation from day 5. RA thrombus resolved by day 31; IVC thrombus resolved by day 16.

Case 3

A 75-year-old male smoker presented post-operatively with dyspnoea after Ray's amputation for diabetic foot ulcer. Raised jugular venous pressure was noted, but ECG was unremarkable. 2D echo revealed an IVC thrombus extending to the tricuspid valve with pulmonary hypertension. Intravenous heparin was initiated, followed by apixaban. IVC thrombus resolved by day 10, and RA thrombus by day 14.

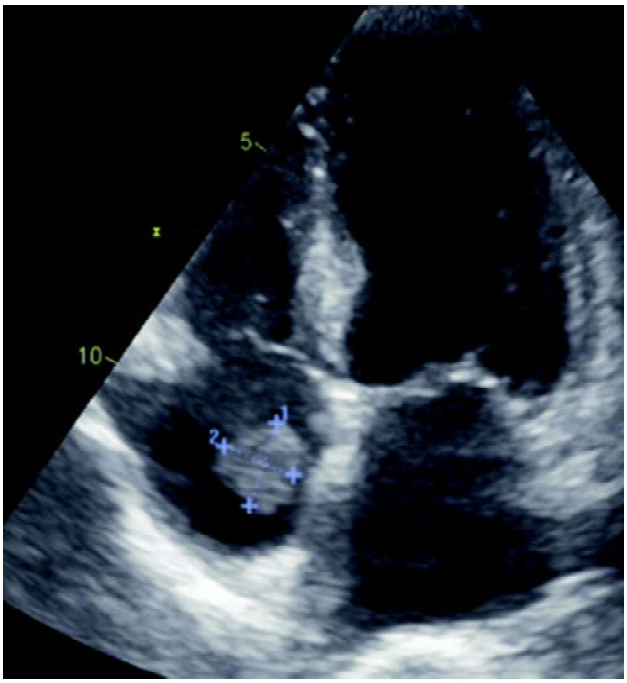

Fig. 3: *Showing thrombus in the right atrium.*

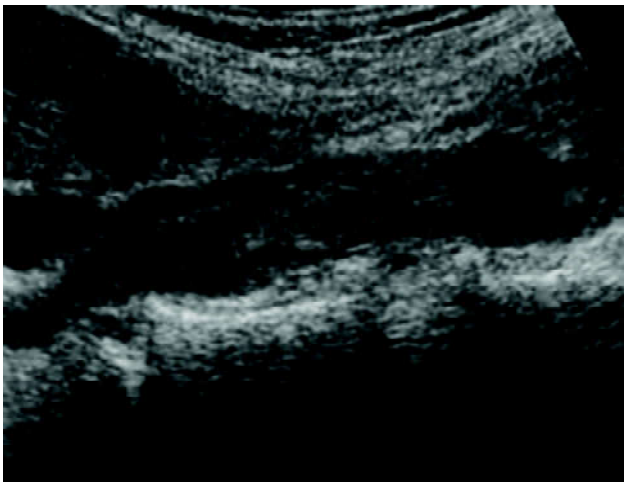

Fig. 4: *Showing IVC thrombus.*

Discussion

Right atrial thrombosis is a rare clinical entity often overlooked in patients with dyspnoea, where attention is frequently directed toward left-sided cardiac pathology. All three patients in this series were elderly male smokers with COPD, fulfilling elements of Virchow's triad through chronic inflammation and potential endothelial dysfunction.

In contrast to reported aetiologies – such as central venous

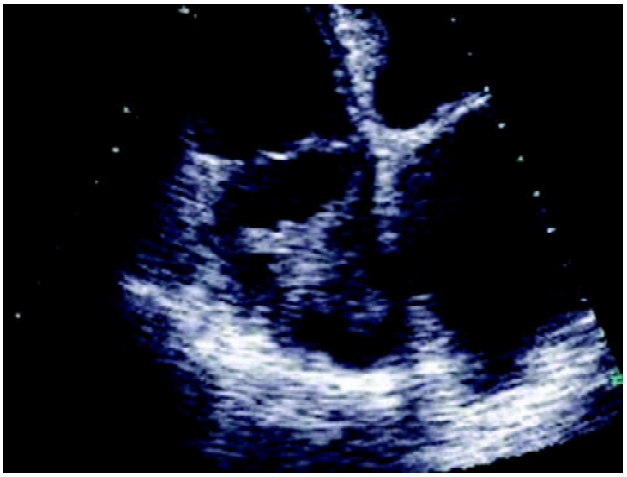

Fig. 5: *Showing thrombus in the right atrium.*

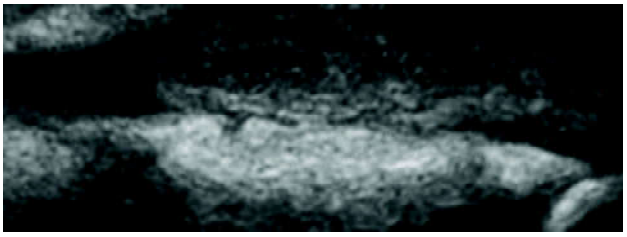

Fig. 6: *Showing IVC thrombus.*

catheter use, pacemaker leads, malignancies, Behcet's disease, and congenital anomalies – none of the patients had these risk factors. Notably, none of the patients required surgical intervention or IVC filter placement. While some studies have reported complications with heparin use in IVC thrombus, all three patients in this series tolerated bridging anticoagulation without bleeding or embolic events.

Due to resource constraints, advanced imaging such as MRCT was not used, though its utility in prognosticating RA thrombus and potential pulmonary embolism is well-established.

These cases suggest COPD-associated chronic inflammation may create a prothrombotic environment sufficient for spontaneous thrombus formation. Conservative anticoagulation may be a viable treatment option in such scenarios.

Conclusion

Right atrial thrombus in association with IVC thrombosis is a rare and often under-recognised cause of acute dyspnoea. This case series underscores the potential role of COPD and smoking in creating a hypercoagulable state. In the absence of traditional risk factors, conservative management with anticoagulation may be effective and safe. Larger cohort studies are warranted to further explore this association and determine optimal management protocols.

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CASE REPORT

JIACM 2025; 26 (3): 140-43

Dengue and Haemophagocytic Lymphohistiocytosis – An Uncommon Sequelae of a Common Disease

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Abstract

Dengue is a viral illness endemic to many parts of India. A lot many complications can arise in dengue in addition to the usual clinical presentation. A 30-year-old male patient presented with prolonged fever, organomegaly and cytopenias. His dengue NS1 antigen was positive. Further evaluation revealed hyperferritinaemia, hypertriglyceridaemia and haemophagocytic lymphohistiocytes on bone marrow studies. A diagnosis of haemophagocytic lymphohistiocytosis (HLH) secondary to dengue fever was made and patient was treated with dexamethasone and etoposide leading to recovery. We intend to highlight the importance of keeping HLH in mind while dealing with patients of dengue fever presenting with prolonged or atypical clinical features.

Key words: Dengue, HLH, cytopenia, hyperferritinaemia.

Introduction

Dengue is an arboviral infection which is endemic in tropical and subtropical geographic locations. It is transmitted from person to person by the bite of mosquitoes belonging to the genus Aedes. Presentations in dengue can vary from asymptomatic infection to severe disease involving various organ systems[1].

Haemophagocytic lymphohistiocytosis (HLH) is a potentially life-threatening disease with a varied aetiology. It is characterised by a wide spectrum of clinical manifestations including fever, cytopenias, organomegaly and nervous system dysfunction. HLH can be either primary or secondary. Primary HLH has a familial or genetic basis while secondary HLH is related to a wide variety of causes including infections, malignancies, autoimmune and metabolic disorders[2].

Dengue fever, as an infectious trigger, has been associated with HLH[3]. This association presents a distinctive challenge to clinical practitioners due to its rarity, speed of progression and coinciding clinical features. Here we present a case of dengue complicated by the development of haemophagocytic lymphohistiocytosis.

Case report

A 30-year-old male patient without any known co-morbidities presented to the emergency with a history of fever since ten days associated with chills and generalised body aches. He had been taking treatment from a local practitioner and had tested positive for Dengue NS1 antigen. On presentation his pulse rate was 108 beats per minute, blood pressure was 100/60 mm of Hg, respiratory rate was 22 beats per minute, temperature was 101° F and oxygen saturation was 98% on room air. On systemic examination liver was palpable 3 cm below the right costal margin and spleen was palpable 4 cm below the left costal margin. Rest of the systemic examination was within normal limits. Investigations revealed a haemoglobin level of 12 g/dL, leucocyte count of 2,540 cells/cumm and a platelet count of 40,000/cumm. Total and direct bilirubin levels were 1.41 and 1.05 mg/dL, SGOT and SGPT were 91 and 38 U/L, ALP was 332 U/L and total protein and albumin levels were 7. 6 and 3.0 g/dL respectively. RFT was within normal limits. He was diagnosed as a case of dengue fever with thrombocytopenia and was started on IV fluids and other supportive treatment. Even after 14 days from the onset of illness, high-grade fever continued along with a progressive decline of haemoglobin levels from 12 g/dL on presentation to 7.4 g/dL along with persistent leucopenia, thrombocytopenia and progressive hepatosplenomegaly. Peripheral blood film examination did not reveal the presence of any atypical cells. There was no evidence of bleeding. This prolonged duration of illness associated with pancytopenia and hepatosplenomegaly warranted a relook into the diagnosis. Keeping a suspicion of HLH in mind patient's serum ferritin and triglyceride levels were measured and they turned out to be significantly elevated (serum ferritin of 2,000 ng/mL and triglycerides of 274 mg/

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dL). A bone marrow examination was performed which showed the presence of haemophagocytic lymphohistiocytes (Fig. 1 given below). A diagnosis of HLH secondary to Dengue fever was made as per the HLH-2004 criteria. The patient was started on Inj. Dexamethasone and Inj. Etoposide . After initiation of treatment, the patient's fever spikes started settling, hepatosplenomegaly started regressing and cell counts started improving. The patient was subsequently discharged in a stable condition. The dose of dexamethasone was tapered and stopped during subsequent visits to the hospital.

Discussion

Dengue is a febrile illness with widely varied clinical presentations. It is one of the major and rapidly expanding mosquito borne viral infections in the world currently. Worldwide incidence of dengue has exponentially increased in the recent decades and nearly half of the world's population is at risk of contracting dengue. It is endemic in tropical and subtropical countries, mostly in the urban and semi-urban settings. Around 100 to 400 million new cases of dengue occur worldwide every year according to conservative estimates[4].

As far as India is concerned, dengue is endemic in almost all states and is an important cause for hospital admissions[5]. As per the census published by the National Centre for Vector Borne Diseases Control, about 2 lakh dengue cases were reported during 2024 in India.

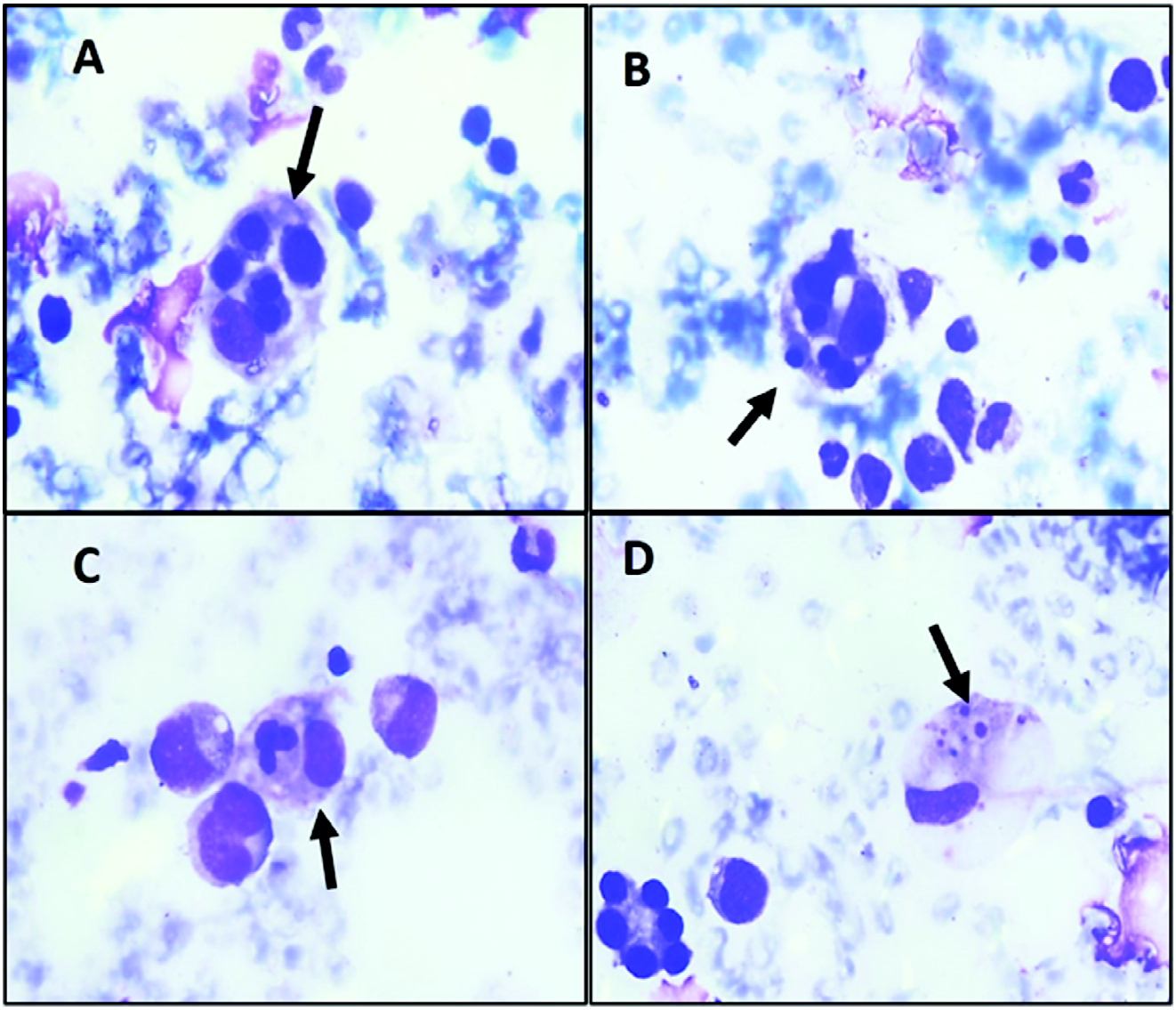

Fig. 1: *Haemophagocytic cells in bone marrow aspirate.* ***A and B:*** *Histocytes engulfing multiple erythroid precursors, MGG, x 1,000.* ***C:*** *Histiocyte with single engulfed Neutrophil, MGG, x 1,000.* ***D:*** *Histiocyte with engulfed Platelets, MGG, x 1,000.*

Dengue virus is transmitted in the community through the bite of infected mosquitoes. The primary vector is Aedes aegypti. Aedes albopictus is a secondary vector of dengue confined to only few regions in the world[1]. Major clinical features include fever, retro orbital pain and myalgias. A typical case of dengue infection passes through three phases, namely febrile, critical and recovery phase. Thrombocytopenia, the hallmark of dengue infection, starts during the febrile phase. The critical phase is characterised by systemic vascular leak and may lead to shock and multi organ dysfunction. The subset of the patients who develop organ failure are referred to as having expanded dengue syndrome. Complications which can arise are numerous and include encephalitis, Guillain-Barré syndrome, hepatitis, pancreatitis, nephritis, myocarditis, myositis and haemophagocytic lymphohistiocytosis[6-9]. The management of dengue is mainly supportive, including intravenous fluids, nutrition and support for specific organ-related complications[10].

Haemophagocytic lymphohistiocytosis is a grave, hyperinflammatory condition which can result in organ failure and death. HLH is classified into two. Primary HLH occurs as a result of inheried genetic mutations and usually presents early in childhood. Secondary HLH occurs due to an abnormal host response to various infections, malignancies or autoimmune disorders and presents in adults associated with an acute illness[11].

The prevalence of HLH in the general population is difficult to ascertain, even more so for secondary HLH. Estimates place it at 1 in 2,000 for adults admitted in critical care settings[12].

The clinical features of HLH are comprehensively covered under the HLH-2004 diagnostic criteria. Diagnosis is established by the presence of at least 5 out of the following 8 criteria – fever, cytopenias, splenomegaly, hypertriglyceridaemia with or without hypofibrinogenaemia, biopsy proven haemophagocytosis, ferritin levels greater than 500 ng/mL, low or absent natural killer (NK) cell activity and elevated soluble interleukin 2 receptor alpha levels greater than or equal to 2,400 U/mL[13]. Our patient had persistent fever, pancytopenia, splenomegaly, hypertriglyceridaemia, hyperferritinaemia and haemophagocytosis on bone marrow biopsy thereby fulfilling 6 out of the 8 criteria.

Pathophysiology of HLH primarily involves an innate immune system dysregulation, specifically involving the NK cells and CD 8+ cytotoxic T-cells. In an intact immune system these cells produce two apoptotic enzymes, namely perforin and granzyme. Perforin forms destabilising pores in the target cell membrane which paves the way for entry of the strongly proteolytic granzyme resulting in death and degradation of the target cell. In patients of HLH this process gets disrupted. In primary HLH, specific genetic mutations account for this disruption, while in secondary HLH it is proposed that a highly immunogenic stimuli such as a virus infected cell or a malignant cell brings about this disruption. This ineffective action of NK cells and CD 8+ cytotoxic T-cells on their targets promotes a vicious inflammatory cycle. A disproportionately large number of cytotoxic cells get recruited but are unable to neutralise the pathologic antigen further resulting in a massive increase in circulating cytokines. Hypercytokinaemia in turn causes widespread macrophage activation and resultant haemophagocytosis and organ damage[14].

The major cytokines implicated are interferon gamma (IFN-α, cytokines tumour necrosis factor alpha (TNF-α), interleukin 1 (IL-1) and interleukin 6 (IL-6). IFN-α and TNF-α act on haematopoetic cells leading to cytopenias. IL-1, IL-6 and TNF-α are implicated as the cause for prolonged fever. TNF-α further inhibits the enzyme lipoprotein lipase leading to hypertriglyceridaemia. The activated macrophages screte ferritin and plasminogen activator resulting in hyperferritinaemia and hypofibrinogenaemia respectively. The elevated number of NK and activated T-cells secrete increased amounts of interleukin 2 receptor alpha[2].

In HLH secondary to dengue, the viral infection triggers excessive cytokine secretion and rampant immune mediated organ destruction[15,16,17].

Treatment of HLH includes immunosuppression and cytotoxic therapy. HLH-2004 criteria recommends an initial 8 week therapy containing dexamethasone and etoposide. Based on individual case scenarios continuation treatment can be provided which includes dexamethasone and etoposide with or without cyclosporine A. Patients with progressive neurological symptoms can be given intrathecal methotrexate. Haematopoetic stem cell transplantation should be provided to patients with familial, relapsing or severe and persistent HLH[18]. This treatment should go hand in hand with treatment for the underlying trigger in cases of secondary HLH.

Patients with dengue associated HLH may not require cytotoxic therapy or stem cell transplantation. Corticosteroids alone can manage this condition many a times[19].

Conclusion

Non-specific clinical presentation and laboratory findings leave HLH underdiagnosed in dengue patients. Fever, pancytopenia and hyperferritinaemia can occur in both dengue and HLH. However, in contrast to patients just having severe dengue, patients with HLH complicated infections

commonly have atypical features such as prolonged fever of more than seven days, hypertriglyceridaemia, hypofibrinogenaemia and haemophagocytosis on bone marrow[19].

Clinicians should have a high index of suspicion for HLH in dengue patients with symptoms and signs out of proportion to the phase of dengue fever. Early identification and treatment initiation forms the cornerstone in the management of this life threatening entity.

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CASE REPORT

JIACM 2025; 26 (3): 144-48

Atypical Adult-Onset Cystic Fibrosis in a Patient with Type 1 Diabetes Mellitus: Diagnostic Challenges with Multisystem Involvement

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Abstract

Cystic fibrosis (CF) is a multisystem autosomal recessive disorder most commonly found in the Caucasian populations, typically diagnosed in childhood. Adult-onset presentations are rare and often misdiagnosed due to overlapping features with other chronic respiratory or gastrointestinal diseases. We present the case of a 19-year-old Indian male who presented with prolonged weight loss, chronic diarrhoea, persistent fever, productive cough, and progressive dyspnoea. His past medical history included type 1 diabetes mellitus, and he was being treated for pulmonary tuberculosis. Clinical evaluation revealed signs of malnutrition, bilateral hearing impairment, and persistent hypokalaemia unresponsive to supplementation. Imaging showed patchy lung consolidation, bronchiectasis, and fibrotic changes. Barter and Gitelman syndromes were suspected due to the unexplained and refractory hypokalaemia but its presence with type 1 diabetes, recurrent pulmonary infections, sensorineural hearing loss, raised suspicion of cystic fibrosis, which was confirmed through genetic testing. This case underscores the importance of considering possibility of cystic fibrosis in the differential diagnosis of chronic respiratory and systemic symptoms in adult patients, particularly in regions where the disease is considered uncommon.

Introduction

Cystic fibrosis is a life-limiting genetic disorder caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, resulting in defective chloride ion transport across epithelial membranes[1,2]. Although it is most frequently diagnosed in early childhood among Caucasians, there is growing recognition globally of adult-onset cystic fibrosis, especially with improved diagnostic awareness and access to genetic testing[3,4]. In adults, clinical manifestations can be atypical and are often misattributed to other more common illnesses, such as asthma, bronchiectasis of other aetiologies, or tuberculosis, particularly in resource-limited settings[5]. Adult patients may present with subtle or single-organ involvement, which delays diagnosis and appropriate intervention[6,7]. This case report discusses an unusual presentation of cystic fibrosis in a young adult male from India, where the disease is underreported and frequently overlooked as it is uncommon in the region[3,5,8].

Case Description

A 19-year-old male presented to our hospital with a one-year history of significant weight loss amounting to 15 kilograms. Over the previous three months, he had been experiencing chronic diarrhoea and, in the last week, reported passage of blood in stool. For the past ten days, he complained of fever associated with night sweats, along with a productive cough yielding yellow sputum and increasing shortness of breath. His dyspnoea had progressed to Modified Medical Research Council (MMRC) grade 3 and was worse in the supine position. His medical history revealed that he had been diagnosed with type 1 diabetes mellitus five years earlier and was on insulin therapy. He had also been diagnosed with pulmonary tuberculosis and was on anti-tubercular therapy, specifically ethambutol and levofloxacin, for the past one month. Social history revealed that he was a chronic smoker and a habitual tobacco chewer.

On examination, the patient appeared cachexic and undernourished. He was afebrile at presentation, with a pulse rate of 92 beats per minute and blood pressure of 102/68 mmHg. Auscultation of the chest revealed bilateral early and mid-inspiratory coarse crepitations along with diffuse rhonchi. Neurologically, the patient reported decrease in hearing, which was confirmed through pure tone audiometry showing severe sensorineural hearing loss in the right ear and mixed severe hearing loss in the left ear.

Laboratory investigations including a complete blood count were within normal limits, with a haemoglobin level of 11.2 g/dL, a white cell count of 7,200/mm^3, and a platelet

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count of 170,000/mm^3. However, serum electrolytes revealed significant hypokalaemia with a potassium level of 2.9 mmol/L, while sodium was 141 mmol/L and chloride was 113 mmol/L. Despite intravenous potassium supplementation, the patient's serum potassium level remained low, and repeated testing on the second day showed potassium at 2.9 mmol/L with sodium at 132 mmol/L and chloride at 109 mmol/L. Further evaluation of hypokalaemia revealed a urine osmolality of 300 mOsm/kg and a serum osmolality of 261 mOsm/kg, with urinary sodium at 113 mmol/L, urinary potassium at 19 mmol/L, urinary chloride at 13 mmol/L,24-hour urinary protein excretion of 70 mg and C-peptide levels as 0.46 ng/mL.

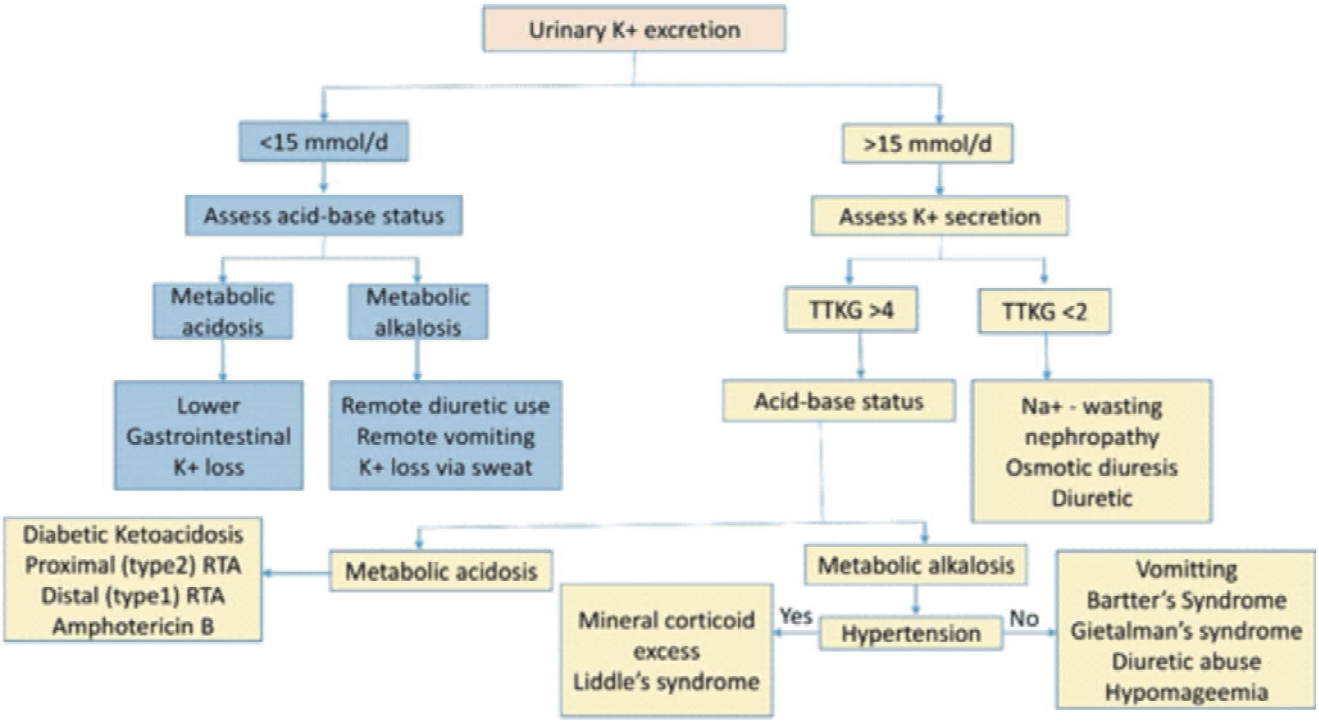
Due to the presence of chronic respiratory symptoms and history of tuberculosis, a chest X-ray AP view was performed. The imaging demonstrated patchy areas of consolidation and collapse in the right upper and bilateral middle lung lobes suggestive of an infective process, along with fibrotic opacities in the upper lobes and evidence of bronchiectatic changes in both lower lobes. This radiological picture, along with clinical findings, suggested a chronic suppurative pulmonary process. The combination of type 1 diabetes mellitus, chronic productive cough, recurrent respiratory infections, and unexplained refractory hypokalaemia led to a suspicion of cystic fibrosis. The presence of sensorineural hearing loss further supported a multisystem disease process.

The patient's urinary potassium excretion was checked and found to be more than 15 mmol/day. Therefore, to proceed with further workup, the trans tubular potassium gradient (TTKG) was calculated by dividing the urine potassium concentration by the ratio of urine to plasma osmolality, which was found to be greater than four. An arterial blood gas analysis was subsequently advised, which revealed metabolic alkalosis. Given the presence of hypokalaemia, urinary potassium excretion greater than 15 mmol/day, a TTKG greater than four, metabolic alkalosis, and a normotensive status, the patient was suspected to have either Gitelman or Bartter syndrome (Flow chart 1).

To confirm the diagnosis, genomic sequencing was conducted, which confirmed the presence of mutations in the CFTR gene, thereby establishing the diagnosis of cystic fibrosis and ruled out Gitelman or Bartter syndromes.

The patient was managed conservatively for hypokalaemia, intravenous cycles of potassium chloride (KCl) were given. After the serum potassium level reached 3.4 mmol/L, he was switched to oral potassium supplementation. For pulmonary tuberculosis, the patient was started on a six-month course of anti-tubercular therapy. For type 1 diabetes mellitus, insulin therapy was continued. In view of sensorineural hearing loss, the patient was advised to use a

Flow chart 1: Clinical approach to Hypokalaemia



hearing aid. Following the confirmation of a diagnosis of cystic fibrosis, Ivacaftor (a CFTR potentiator, improving the function of protein in the body to decrease the build-up of thick mucus in lungs and improving the symptoms of cystic fibrosis) twice daily was initiated. Additionally, chest and limb physiotherapy, along with cough expectorants, were administered.

The patient was discharged with these medications. On follow-up after 7 days, the serum potassium level had improved, but blood glucose levels remained uncontrolled, which was further managed by adjusting the insulin dose. On the next follow-up after 1 month, the patient's serum potassium levels and blood glucose levels were checked again, and an X-ray was repeated, which showed improvement in serum potassium levels and control of blood glucose levels, along with improvement on the X-ray. The patient was continued on the same medication.

Case Discussion

This case highlights the diagnostic complexity and clinical significance of atypical presentations of cystic fibrosis (CF), particularly in a young adult male from India – a region where CF is considered rare and often underdiagnosed[3,5,8]. Traditionally viewed as a pediatric disease with early-onset symptoms, CF is increasingly being recognised in adolescents and adults due to better diagnostic techniques and improved clinical awareness[3,4]. However, late-diagnosed cases often have milder or non-classical presentations, making diagnosis challenging, especially in areas with high prevalence of diseases that mimic CF, such as tuberculosis[4,5].

The patient's initial clinical presentation raised a broad range of diagnostic possibilities. He had constitutional symptoms including chronic weight loss, low-grade fever, productive cough, and breathlessness. These findings, combined with radiologic features such as consolidation and fibrotic changes, led to a preliminary diagnosis of pulmonary tuberculosis. This was a reasonable first impression given his demography and the high endemicity of tuberculosis in the region[5]. The patient had also been on a course of anti-tubercular therapy which caused ATT-induced hepatitis, so patient was started on Ethambutol and Levofloxacin, but his lack of clinical improvement and the persistent progression of symptoms prompted further investigations. However, tuberculosis alone could not explain the full spectrum of his systemic symptoms. Chronic diarrhoea, persistent hypokalaemia, and sensorineural hearing loss pointed to a more complex and multisystem pathology. Inflammatory bowel disease and celiac disease were considered due to the gastrointestinal symptoms and nutritional deficiencies. Yet, neither accounted for the patient's respiratory involvement or persistent metabolic derangements.

Renal tubulopathies such as Bartter or Gitelman syndromes were also explored due to the recurrent, treatment-resistant hypokalaemia and trans tubular potassium gradient (TTKG) more than four. These conditions are known to cause potassium and chloride wasting, metabolic alkalosis, with normotension. But, the biochemical profile did not fully align, and these syndromes do not typically present with concurrent pulmonary, gastrointestinal, and endocrine abnormalities. Moreover, the patient's serum and urine osmolality values and urinary electrolytes suggested renal salt loss in the context of a systemic condition rather than an isolated renal disorder.

Another consideration was a mitochondrial cytopathy, given the constellation of diabetes, hearing loss, and multisystem involvement. However, the absence of neurological signs, lactic acidosis, or maternal inheritance pattern made a mitochondrial disorder less likely. Primary immuno-deficiencies, such as common variable immunodeficiency (CVID), can present with recurrent respiratory infections and gastrointestinal symptoms. Still, there was no history of frequent infections in early life or laboratory evidence of immune deficiency, making this diagnosis unlikely.

Ultimately, a unifying diagnosis was achieved with CFTR gene mutation testing, confirming cystic fibrosis[3,6]. This diagnosis brought clarity to the patient's complex presentation. The gastrointestinal complaints and malnutrition were attributable to pancreatic exocrine insufficiency, a classic but sometimes overlooked feature of CF, particularly in adults[1,2,6]. His diabetes was consistent with cystic fibrosis-related diabetes (CFRD), which is distinct from type 1 and type 2 diabetes. CFRD arises from pancreatic islet cell destruction and insulin resistance due to chronic inflammation and fibrosis. This patient had low C-peptide levels and elevated HbA1c levels and in CFRD C-peptide levels are either elevated or normal and HbA1c levels are either low or normal. Therefore, the patient was labelled as having type 1 diabetes mellitus[1]. CFRD affects approximately 40 - 50% of adults with CF and is associated with worse pulmonary function and nutritional outcomes[1].

The hypokalaemia, which was refractory to oral supplementation, was explained by a salt-losing syndrome secondary to CF[2,6]. The defect in chloride transport results in renal and sweat gland salt wasting. Diarrhoea, insulin use, and malabsorption compounded these losses, as reflected in his abnormal urinary and serum electrolyte levels. Persistent hypokalaemia in young patients, especially when associated with multisystem findings, should prompt evaluation for CF, particularly when more common causes have been excluded[6].

The sensorineural hearing loss observed in this patient is not a direct consequence of CF pathology but is an important clinical clue. CF patients often experience chronic otitis media due to Eustachian tube dysfunction or may develop hearing impairment secondary to ototoxic antibiotics, particularly aminoglycosides, which are commonly used to manage bacterial lung infections. In our patient, there is no history of aminoglycosides administration[7].

A striking aspect of this case is the diagnostic delay caused by geographic and epidemiologic biases. In South Asia, CF remains under-recognised due to its perceived rarity, lack of widespread new-born screening, limited access to sweat chloride testing, and a general underappreciation of adult-onset or atypical cases[3,5,8]. Furthermore, the genetic profile of CFTR mutations in South Asian populations differs from Western cohorts, with a lower prevalence of the common AF508 mutation and a higher frequency of rare or region-specific variants[3,8]. This genetic variability likely contributes to milder or variable phenotypes and complicates standard diagnostic pathways.

Several critical clinical lessons emerge from this case. Firstly, clinicians must suspect for CF in young or adults who present with type 1 diabetes mellitus, chronic productive cough, recurrent respiratory infections, and unexplained hypokalaemia. Secondly, the presence of persistent hypokalaemia should prompt consideration of systemic conditions like CF when more common renal, endocrine and gastrointestinal causes have been ruled-out[6]. Thirdly, the co-existence of chronic pulmonary disease and diabetes mellitus in a young patient should be a red flag, especially in the context of weight loss and malnutrition[1,6]. Finally, this case reinforces the value of molecular genetic testing in confirming CF, especially in atypical presentations or in resource-constrained settings where traditional diagnostics like sweat chloride testing may be unavailable or inconclusive[3,6].

In conclusion, this case not only broadens the clinical spectrum of adult-diagnosed CF but also serves as a reminder of the diagnostic challenges posed by systemic diseases with overlapping features. It underscores the importance of holistic patient evaluation, context-specific diagnostic algorithms, and the critical role of genetic testing in achieving diagnostic clarity. Heightened awareness and early recognition are essential to avoid delays in appropriate management and to improve long-term outcomes in patients with atypical CF[3,5].

Review of Literature

Cystic fibrosis (CF), historically considered a paediatric disease, is now increasingly recognised in adults due to greater awareness, improved diagnostic tools, and milder phenotypic variants. Barry and Simmonds (2023) emphasized that adult presentations are often atypical and may involve subtle or organ-specific symptoms such as recurrent sinusitis, pancreatitis, or male infertility. Delayed diagnosis in adults can be attributed to retained pancreatic function and less severe pulmonary manifestations, making comprehensive diagnostic workup – including sweat chloride testing, CFTR mutation analysis, and nasal potential difference studies – essential for confirmation[4].

A recent study by Vaidyanathan *et al* (2022) highlighted significant disparities in the diagnosis and treatment of cystic fibrosis (CF) among Asian populations, using data from major international CF registries. The authors found that Asian individuals are underrepresented in CF registries and frequently harbour rare or population-specific CFTR mutations not covered by standard Western mutation panels. This genetic diversity complicates diagnosis, leading to under diagnosis or misdiagnosis. Furthermore, limited representation in clinical trials restricts access to CFTR modulator therapies for many Asian patients. The study underscores the urgent need for inclusive genetic screening protocols, population-specific mutation databases, and equitable access to precision therapies across all ethnic groups[3].

Mandal *et al* (2015) examined the Indian context, highlighting that CF is often underdiagnosed or misdiagnosed due to limited awareness and access to diagnostic facilities. The clinical phenotype in Indian patients is typically severe, with earlier colonisation by Pseudomonas aeruginosa, significant malnutrition, and frequent vitamin deficiencies. The review also pointed out the relatively lower frequency of the AF508 mutation in the Indian population, complicating genetic confirmation of the disease[8].

The American Diabetes Association's 2010 standards provide comprehensive guidelines for the management of diabetes, including diagnostic criteria, glycaemic targets, and complication monitoring. While not CF-specific, these guidelines are highly relevant for managing cystic fibrosis-related diabetes (CFRD), a common comorbidity in adult CF patients, which requires an individualised approach due to overlapping features of both type 1 and type 2 diabetes[10].

Kabra *et al* (2003) presented data from a cohort of North Indian children with CF, underlining the burden of delayed diagnosis and associated complications such as severe malnutrition, fat-soluble vitamin deficiencies, and chronic respiratory infections. They stressed the need for increased clinical suspicion in children with recurrent respiratory or gastrointestinal symptoms, even in populations where CF is considered rare[11].

Collectively, these studies underscore the diagnostic and therapeutic challenges associated with CF in resource-limited settings and adult populations. They also highlight the importance of multidisciplinary care, especially in patients with overlapping co-morbidities such as diabetes and chronic infections.

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CASE REPORT

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Rare Survival from Paraquat Poisoning: 'A Case Report'

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Abstract

Paraquat is a highly toxic herbicide which is most commonly used in agriculture to kill weeds. Paraquat (bipyridyl) is a corrosive liquid which is green in colour with pungent smell. This is a case report of a 26-year-old male, who was admitted in SVBP Hospital emergency with history of alleged intake of paraquat poison. On admission, the patient was in severe respiratory distress. Due to prompt and aggressive management, the patient improved and got discharged. Although there is no proper management protocol and antidote available for managing paraquat poisoning, proper strategies and effective management of ARDS, along with early intervention to prevent complications is the key to patient survival .

Key words: Paraquat poisoning, ARDS.

Introduction

Paraquat, whose chemical composition is 1,1-dimethyl-4, 4 bipyridyl dichloride, is commonly used herbicide in agriculture because it is rapidly inactivated in soil. It prevents photosynthesis in plants by interfering with ETC (electron transport chain). It is green coloured liquid which often is fatal on ingestion. When paraquat is taken orally , it causes release of hydrogen and *superoxide* anions. These anions cause lipid damage in the cell membrane and lead to pulmonary fibrosis, hepatotoxicity, and nephrotoxicity[4]. Paraquat exposure has a high case fatality rate of up to 68 - 74%[1]. It presents with a wide variety of clinical symptoms including nausea, vomiting, dyspnoea, oral ulcers (characteristically called as paraquat tongue, which are mucosal lesions in the oral cavity)[2]. Additional symptoms like abdominal pain, diarrhoea, altered mental status and malaena has been reported in some cases[2].

The primary organs affected by paraquat poisoning are the lungs and kidneys. Its chemical resemblance to polyamines facilitates its uptake by the alveolar cells. Additionally, the kidneys actively secrete paraquat, resulting in its accumulation within the proximal tubular epithelial cells. When paraquat accumulates in the pulmonary alveoli and nephrons, it induces redox cycling and generates harmful reactive oxygen species. This oxidative stress surpasses the cellular defense mechanisms, leading to pulmonary injury characterised by alveolitis and fibrosis, which arises from the proliferation and differentiation of fibroblasts[1]. It causes pulmonary fibrosis, hepatic toxicity and nephrotoxicity by free radical damage. There is currently no antidote available and only supportive management is provided.

Case Summary

A 26 years male with an alleged history of parquat ingestion presented to us with chief complaints of pain abdomen, breathlessness and vomiting. Patient was referred from district hospital, Amroha, 4 hrs after the ingestion of approximately 30 to 40 mL of a 20% paraquat solution as suicidal attempt. On examination, patient had tachypnoea and was using his accessory respiratory muscles. His vitals on presentation were: BP - 158/96 mmHg, PR - 98 bpm, SpO2 - 88% on room air. His random blood sugar was 111 mg/dL. On local examination, oral ulcers were observed with characteristic paraquat tongue (Fig. 2). On respiratory system examination, crepitations were present more on the right side of chest in the infra-axillary and mammary area, and on left side only basal crepitations were present. On abdominal examination, mild epigastric tenderness was present. Patient also had decreased urine output of 500 mL/24 hr. On investigations, ABG analysis showed mild hypoxaemia with PaO_2 of 81 mmHg, PH 7.4, and HCO_3 - 22.9 meq/L with serum lactate - 1.1 meq/L (Fig. 3). The bicarbonate PaO_2/FiO_2 ratio on presentation was approximately 180, indicating moderate ARDS. The ROX index calculation was also suggestive of respiratory compromise. Aspartate transaminase (AST) and alanine transaminase (ALT) levels were 20 and 36 U/l, respectively; serum creatinine and blood urea levels were 2.4 mg/dL and 144 mg/dL, respectively. Chest X-ray (PA view) on the day of admission showed bilateral basal haziness and some fibrotic changes more on right side with heterogenous opacity over right lower zone (Fig. 1). High resolution CT scan of the chest was done, which revealed bilateral ground-glass opacities and consolidation.

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Complete haemogram showed mild leuocytosis with TLC - 11,980 cells/dL, haemoglobin of 12.6 g/L and platelet count of 154,000 per cumm. Patient was shifted to ICU, gastric lavage was done with normal saline and activated charcoal (1 gm/kg). As there was no dermal exposure, hence dermal decontamination was not required. For management of respiratory distress, patient was managed conservatively on intermittent Bi PAP along with methylprednisolone 500 mg iv, tab. cyclophosphamide and antioxidant (NAC and vitamin E 800 mg TDS vitamin C - 500 mg BD, glutathione 50 mg BD). Immunosuppression therapy along with antioxidants were given in accordance with Dinis-Oliveira recommendations. Nephrology consultation was taken in view of acute kidney injury, along with strict monitoring of urine output. Haemodialysis was not initiated due to improving renal functions. Patient was closely monitored with hourly blood pressure and oxygen saturation monitoring, daily kidney function tests, and serum electrolytes. ABG analysis was done every 4 hourly. Patient showed gradual improvement with better renal and hepatic profile, improved oxygenation with saturation of 93% on minimum oxygen requirement (1 L/min oxygen) by nasal prongs. On day 2, ABG revealed mild partially compensated metabolic acidosis with some hypoxaemia PH - 7.32, PaO_2 - 98 mmHg, HCO_3 - 21. Serial renal function tests showed improvement and ABG also reflected improved

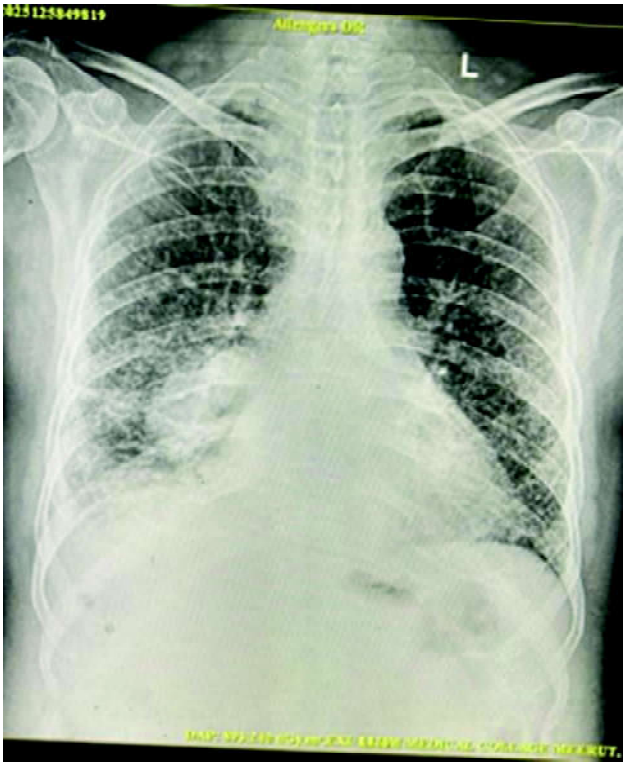

Fig. 1: *Chest X-ray showing bilateral basal haziness and heterogenous opacity over right lower zone.*

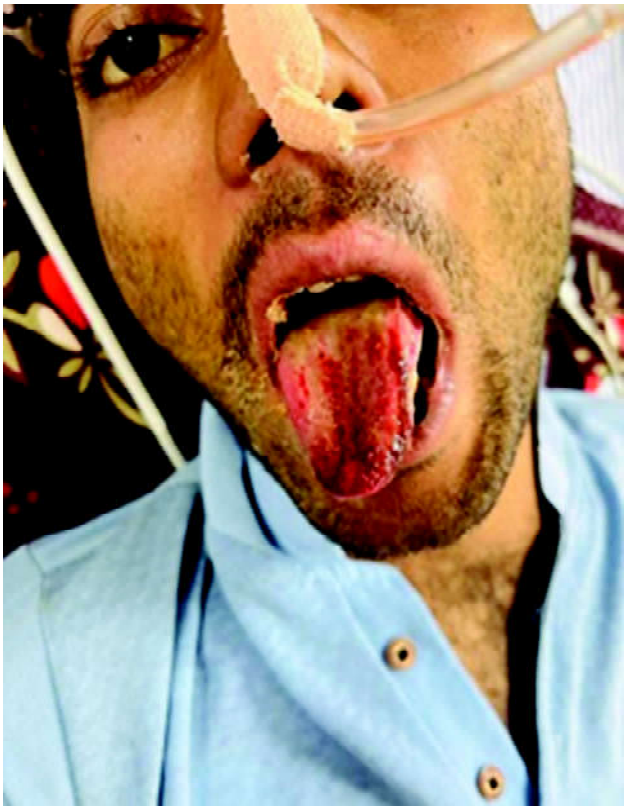

Fig. 2: *Paraquat Tongue.*

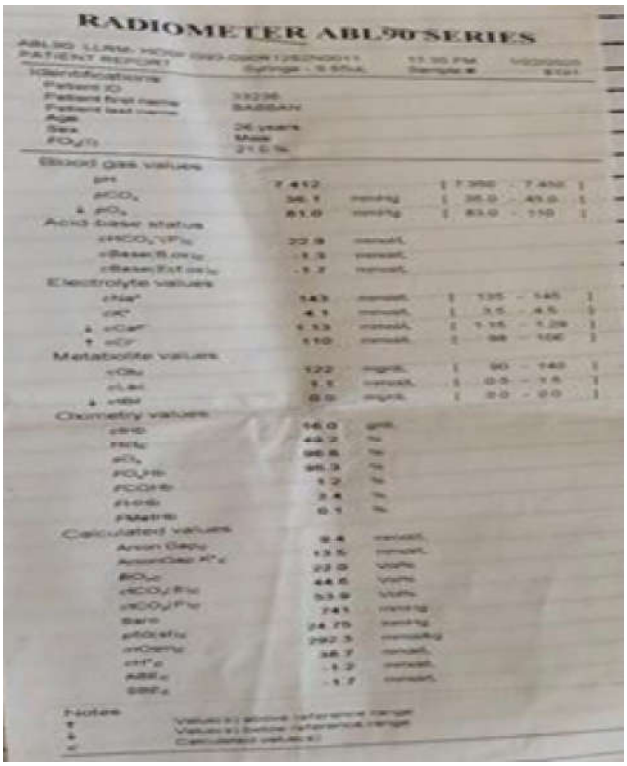

Fig. 3: *ABG report.*

oxygenation status with improvements in lactate levels. He maintained oxygen saturation on intermittent oxygen support of 1 - 2 L/min on nasal prongs. Patient continued to show further clinical improvement and was discharged on day 5.

Discussion

Paraquat when taken orally is highly toxic therefore, it has been classified as "restricted use herbicide". GI decontamination is most effective when done within one hour of exposure, but our patient was a referred case, and he reported to us after 4 hours. Even though there is less benefit of GI decontamination after 3 to 4 hours, we decided to do gastric lavage with charcoal as it was not clear from the referral whether it was done at the primary health centre. There was no dermal exposure in our case so dermal decontamination was not required. Paraquat causes release of super oxide anions which cause lipid damage of the cell membranes in the lungs in the form of pulmonary congestion and fibrosis. In our case also, pulmonary involvement was present in the form of breathlessness, increased respiratory rate, crepitations in mammary and infra-axillary areas with consolidation on chest X-ray, as paraquat has high affinity for alveolar type 1 and type 2 cells. Its concentration in lungs is 10 - 20 times greater than in plasma[5]. Excessive oxygen supplementation should be avoided in paraquat poisoning, as it can increase reactive oxygen species (ROS) production. Therefore, we should provide minimal required oxygen therapy to avoid further free radical injury. Paraquat causes local toxicity in the tongue, oral mucosa like a corrosive injury which was also present in our case (Fig. 2). Renal tubular necrosis due to free radical damage can cause nephrotoxity, though in our case there was only minimal involvement of kidneys in the form of decreased urine output which was improved on conservative management[6]. The best predictor of survival after ingestion is calculated from the time of ingestion and the start of treatment, and also the concentration of paraquat in plasma. The index is calculated by multiplying the time from parquat ingestion to the start of treatment.

Conclusion

Paraquat is highly toxic poison which predominantly affects the vital organs. As there is no specific antidote available, so supportive care focusing on prevention of free radical injury and airway protection are of paramount importance. Paraquat is banned in Europe, so we also recommend strict monitoring in India, to limit its misuse. Timely intervention and awareness can prevent many deaths.

Limitations

There was certain limitation in our report like paraquat levels in plasma and urine were not measured, as this test is not available in our institute.

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CASE REPORT

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Autoimmune Haemolytic Anaemia as an Unusual Presentation of Brucellosis in a Middle-Aged Woman

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Abstract

Brucellosis, a widespread zoonotic infection in developing countries, frequently presents with nonspecific symptoms, complicating its diagnosis. This report highlights a rare case of brucellosis in a 42-year-old woman with a prosthetic mitral valve, who presented with Coombs-positive haemolytic anaemia, though the peripheral blood film showed no schistocytes. Her symptoms included low-grade fever, shortness of breath, dry cough, and weakness. Laboratory tests confirmed hemolysis, and blood cultures identified Brucella melitensis as the causative pathogen. The patient was successfully treated with a prolonged course of doxycycline and rifampicin. This case emphasizes the importance of considering brucellosis in the differential diagnosis of haemolytic anaemia, particularly in endemic regions.

Key words: Brucellosis, haemolytic anaemia, Coomb's test, prosthetic mitral valve, zoonosis.

Introduction

Brucellosis, also known as Malta fever or Mediterranean fever, is a common zoonotic disease in many developing countries. It is caused by gram-negative coccobacillus, of which, *B. melitensis* and *B. abortus* affect humans most commonly. The infection is transmitted to humans via direct contact with infected animals or consumption of unpasteurised dairy products[1,2,3]. The constitutional symptoms occur in both acute and chronic infections. however, they are more frequent in acute infection[1,4]. Fever occurs during the disease in almost all patients[1]. Though primarily known for its systemic and musculoskeletal manifestations, it can present atypically with haematologic abnormalities, including pancytopenia, thrombocytopenia, and rarely, haemolytic anaemia[5,6,7]. The rarity of such presentations often delays diagnosis[8,9].

We report a rare presentation of brucellosis in a middle-aged woman with prosthetic mitral valve, who presented with haemolytic anaemia and fever – initially without any specific localizing signs – highlighting the diagnostic challenge and the need for high clinical suspicion in endemic regions[10].

Case Presentation

A 42-year-old female presented to the hospital with symptoms of low-grade fever for 40 days, shortness of breath on exertion for 30 days, dry cough for 30 days, and generalised weakness for 20 days. The patient had undergone mitral valve replacement 4 years back and was on long-term anticoagulation therapy with acenocoumarol, along with aspirin and torsemide. Her occupational background as a farmer exposed her regularly to cattle and unpasteurised milk. She had no history of smoking, alcohol use or recent travel.

On physical examination, she was febrile with temperature of 101.2° F, tachycardic (pulse rate 102 bpm), and normotensive (BP 110/70 mmHg), with oxygen saturation of 96% on room air. Pallor was present, but there were no signs of icterus, lymphadenopathy or oedema. Cardiovascular examination revealed a metallic S1 click consistent with her prosthetic valve, without any murmurs. Respiratory and central nervous system examination was unremarkable, while abdominal examination revealed mild hepatomegaly. Initial laboratory workup showed microcytic hypochromic anaemia, and peripheral smear confirmed anisocytosis and polychromasia with no parasitic forms and adequate platelet count. A positive direct Coomb's test, elevated ESR- 85mm\h, and signs of ongoing hemolysis pointed towards immune-mediated haemolytic anaemia. Chest X-ray findings were normal, and 2D echocardiography revealed a well-functioning prosthetic mitral valve with no vegetations or features suggestive of infective endocarditis. Blood culture grew *Brucella melitensis* species, confirming the infectious aetiology.

With a final diagnosis of brucellosis-associated Coomb's-positive haemolytic anaemia, the patient was initiated on oral doxycycline 100 mg twice daily and rifampicin 600 mg

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once daily for a total of 6 weeks. Supportive treatment included transfusion of two units of packed red blood cells, folic acid, and oral iron supplementation. Anticoagulation with acenocoumarol was continued with regular INR monitoring and dose adjustments. The patient showed a favourable response, with defervescence of fever by the fourth day of treatment and progressive improvement in haemoglobin levels following transfusion. Repeat blood cultures taken after 2 weeks of initiation of antibiotics were sterile. She was discharged on the seventh day with instructions for outpatient follow-up focusing on anticoagulation management and haematologic monitoring. At her four-week follow-up, she remained afebrile, her energy levels had returned to normal, and her haemoglobin had improved to 11.8 g/dL.

Discussion

Brucellosis is a globally prevalent zoonotic disease caused by Brucella species, *primarily B. melitensis*, which infects humans through direct contact with infected animals or the ingestion of unpasteurised dairy products[1,2]. It remains endemic in India, especially among individuals involved in livestock handling or rural occupations[3,4]. The disease often presents with non-specific symptoms such as fever, malaise, and fatigue, making the diagnosis challenging[8]. Although brucellosis is known to cause haematologic abnormalities like anaemia, leukopenia, and thrombocytopenia. Autoimmune haemolytic anaemia (AIHA) is a particularly rare manifestation[5,11].

Anaemia in brucellosis is commonly mild and normocytic, associated with chronic disease or bone marrow suppression[8]. However, AIHA, confirmed by a positive direct Coomb's test and features of haemolysis, is exceedingly rare. It is estimated to occur in less than 1% of cases, with fewer than 20 well-documented reports worldwide[5,10,11]. Studies such as Kaya *et al* found anaemia in 13% of patients, but no cases of AIHA in a large cohort[5]. The pathogenesis of AIHA in brucellosis is thought to involve molecular mimicry or immune dysregulation, where Brucella antigens may stimulate autoantibody production against erythrocytes.

Review of literature

Isolated case reports by Meena *et al* and Sari *et al* have described instances of acute brucellosis presenting with Coomb's-positive AIHA, highlighting the diagnostic challenge posed by such atypical presentations[7,11].

Ibrahim *et al* documented a similar case in a Saudi woman, thereby contributing to the limited global literature on this uncommon clinical presentation[10].

Our patient, with a history of mitral valve replacement and occupational exposure to cattle and unpasteurised milk, presented with features of haemolytic anaemia and a positive Coomb's test, eventually confirmed to have Brucella bacteraemia. The presence of a prosthetic valve initially raised concerns for infective endocarditis – a known, albeit rare, complication of brucellosis[6]. However, echocardiography showed a well-functioning prosthetic valve with no vegetations, helping to rule-out endocarditis. Such patients; however, require ongoing monitoring due to the elevated risk of developing prosthetic valve infections[7].

The diagnosis in this case was established via blood culture, which remains the gold standard for detecting *Brucella spp*. Despite requiring prolonged incubation, culture confirms active infection and supports targeted antimicrobial therapy[1]. Serological tests and PCR, though helpful, are often unavailable in many settings. The cornerstone of treatment for brucellosis includes combination antibiotic therapy. The World Health Organisation recommends doxycycline and rifampicin for at least six weeks to prevent relapse[2] . Our patient responded well to this regimen, with resolution of fever by day four and normalisation of haemoglobin levels following transfusion support.

In most reported cases of brucellosis-induced AIHA, supportive treatment with folic acid, iron, and blood transfusions suffice and mainstay treatment of brucellosis include doxycycline, rifampicin, streptomycin and ceftriaxone. Corticosteroids are reserved for severe or refractory hemolysis, and immunosuppressive agents like rituximab or IVIg are rarely required[11]. Given our patient's prosthetic valve, anticoagulation was continued with careful INR monitoring, which was crucial to avoid thrombotic complications.

This case reinforces the importance of considering brucellosis in the differential diagnosis of AIHA in endemic regions. It also highlights the need for early microbiological confirmation, especially in atypical presentations. In patients with prosthetic valves, ruling out endocarditis is critical, and a multidisciplinary approach ensures safe and effective care.

Conclusion

This case highlights a rare presentation of brucellosis as Coomb's-positive autoimmune haemolytic anaemia (AIHA) in a patient with a prosthetic mitral valve, emphasizing the diagnostic challenges associated with its protean manifestations. In endemic regions, brucellosis should be considered in the differential diagnosis of unexplained haemolytic anaemia, particularly in individuals with occupational exposure to livestock or unpasteurised dairy products. Early recognition through appropriate diagnostic

modalities, including blood cultures and Coomb's testing, is essential for prompt treatment and favorable outcomes. The case also underscores the importance of thorough clinical evaluation in patients with prosthetic valves to rule-out infective endocarditis, which remains a significant potential complication. Multidisciplinary management and close follow-up are vital to ensure both infection resolution and stable anticoagulation in patients with cardiac prostheses.

In conclusion, this case contributes to the limited but growing literature on brucellosis-induced AIHA and reinforces the importance of considering infectious etiologies in atypical haematologic presentations, especially in patients with identifiable risk factors such as rural occupation, animal contact and use of unpasteurised milk.

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CASE REPORT

JIACM 2025; 26 (3): 155-56

Dengue Fever Presenting with Acute Appendicular Perforation

Aditya Goyal, Jatin Tewatia*, Esha Singhal**, Bhumesh Tyagi**, Suresh Babu Gupta****

Abstract

Dengue fever has a wide spectrum of gastrointestinal manifestations, ranging from mild discomfort to severe complications. Rarely, it may present with or mask acute surgical emergencies such as appendicitis or appendicular perforation. We present a rare case of a 14-year-old male with dengue infection who developed acute appendicular perforation, successfully managed with emergency appendectomy. This highlights the importance of considering surgical causes of abdominal pain in dengue patients.

Case Report

A 14-year-old boy presented with high-grade fever, vomiting, and progressive abdominal pain. He had no significant co-morbidities. Dengue NS1 antigen and IgM antibodies were positive. Laboratory evaluation revealed thrombocytopenia and elevated liver enzymes. Despite supportive management, the abdominal pain worsened and peritoneal signs appeared. Radiological evaluation showed free intraperitoneal air and free fluid. A diagnosis of acute perforative peritonitis was made, and emergency appendectomy was performed. The postoperative course was uneventful. The patient was treated with intravenous antibiotics, improved clinically, and was discharged in stable condition on the fifth post-operative day.

Laboratory and Histopathology Findings

Histopathology (Excised Appendix) - Gross: Appendectomy specimen measuring 8 cm x 2.5 cm, lumen filled with fecolith.

Microscopy: Appendix lined by intact mucosa. Submucosa showed proliferating blood vessels and dense chronic inflammatory infiltrate comprising lymphocytes and plasma cells. Serosal surface demonstrated necrosis with acute inflammatory exudate.

Impression: Acute appendicitis with periappendiceal abscess.

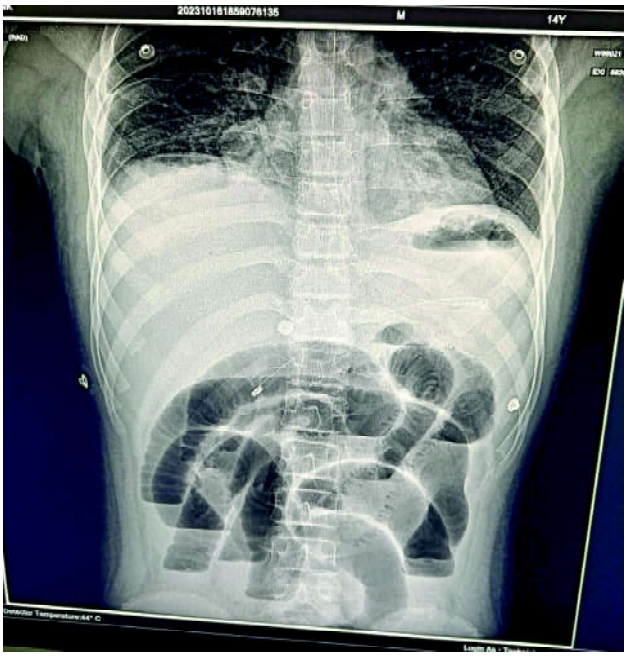

Fig. 1:

Discussion

Dengue infection is endemic in tropical regions and frequently affects the gastrointestinal system. Most manifestations are mild; however, rarely, true surgical emergencies like appendicitis or perforation may occur, posing diagnostic challenges due to overlapping symptoms with viral illness. The likely mechanisms include viral-induced immune dysfunction, vascular leak, ischaemia, and bowel wall edema leading to obstruction and infection. In this case, the progression of abdominal pain, to perforation peritonitis and then to appendectomy was seen. Few paediatric cases of dengue-associated appendicitis or perforation are reported in the literature. Awareness and timely surgical referral are crucial, as delaying intervention may result in sepsis and poor outcomes.

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PICTORIAL CME

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Severe Immune Thrombocytopenic Purpura with Life-threatening Bleeds: A Rare Presentation of Disseminated Tuberculosis

Abrar Hussain, Vishwa Golyan*, Prabhat Kumar***

Introduction

Immune Thrombocytopenic Purpura (ITP) is an acquired autoimmune disorder characterised by isolated thrombocytopenia due to accelerated platelet destruction and impaired platelet production. While ITP is often idiopathic, secondary causes such as autoimmune diseases, malignancies, viral infections, and, rarely, tuberculosis (TB) have been reported. Herein, we present a rare case of severe ITP secondary to disseminated tuberculosis causing life-threatening bleeds which showed dramatic improvement following anti-tubercular therapy (ATT) and steroids[1].

Case Report

A 33-year-old male presented to the emergency department with the complaints of multiple rash over the body for 7 days, black coloured stools for 5 days and 1 episode of generalised tonic clonic seizure. There was history of significant weight loss and anorexia. The patient had tachycardia with a pulse rate of 110/min; blood pressure was 96/60 mm of Hg and the patient was restless and agitated. General physical examination revealed pallor and petechial rash over chest (Fig. 1). Blood investigations revealed low haemoglobin 4.5 g/dL, MCV of 64 fl, thrombocytopenia with a platelet count of 3,000 per cu mm and iron deficiency anaemia with a serum iron of 10 micrograms/dL. Peripheral smear revealed microcytic hypochromic anaemia with severe thrombocytopenia. Human immunodeficiency virus (HIV), Hepatitis B surface antigen (HBsAg), Hepatitis C virus antibody test and antinuclear antibody test were negative. Non contrast CT head revealed left frontal intracerebral haemorrhage (Fig. 2). Chest X-ray revealed widened mediastinum with ill-defined bilateral costophrenic angles (Fig. 3). Upper GI endoscopy revealed erosive gastropathy (Fig. 4). CECT chest and whole abdomen revealed "tree-in-bud" appearance with multiple enlarged conglomerated mediastinal, left-sided pleural effusion, periportal and peripancreatic nodes along with moderate ascites and omental thickening (Fig. 5). Ascitic fluid anothers was done which was lymphocyte

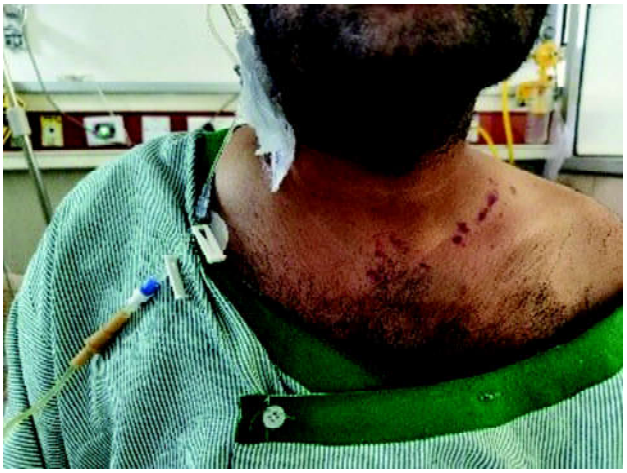

Fig. 1: *Petechial rashes over chest.*

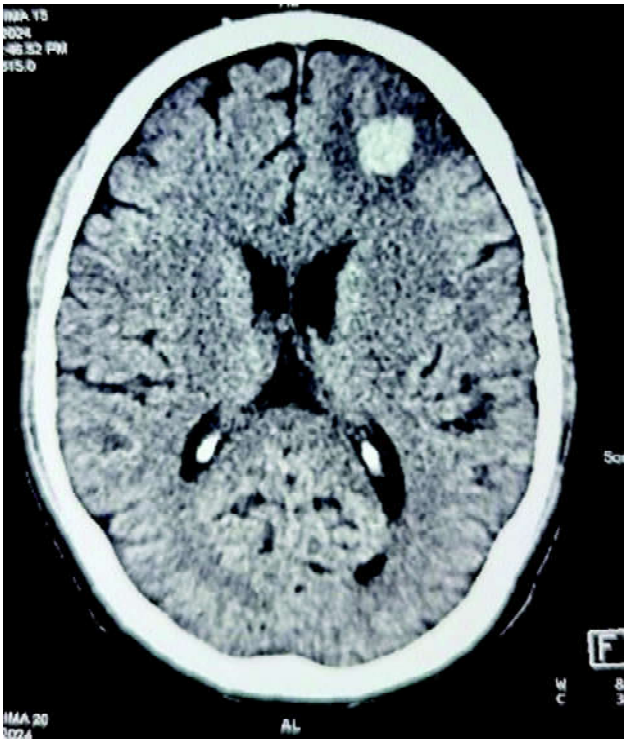

Fig. 2: *CT head showing left frontal ICH.*

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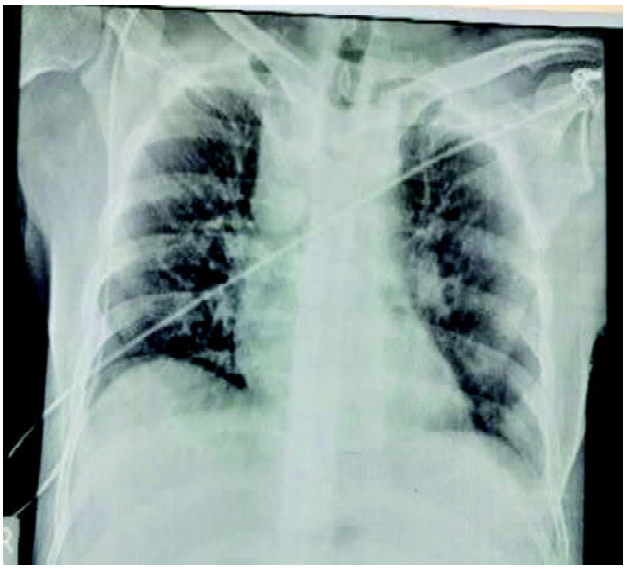

Fig. 3: *CXR showing mediastinum widening.*

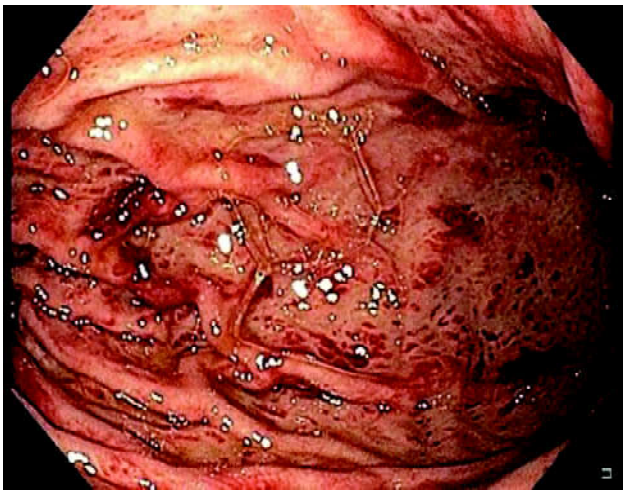

Fig. 4: *Erosive gastropathy on upper GI endoscopy.*

rich exudative fluid with a serum ascites albumin gradient of 0.72 gm/dL with raised adenosine deaminase (ADA) levels of 81.1 U/L. Bone marrow biopsy showed erythroid hyperplasia and was negative for GeneXpert.

A diagnosis of Severe Immune Thrombocytopenia (ITP) secondary to disseminated tuberculosis causing intracerebral haemorrhage and severe gastrointestinal bleed was made. The patient was initially treated with pantoprazole infusion, levetiracetam, IV immunoglobulins 1 gm/kg (for 1 day) along with PRBC and SDP transfusion Intracerebral bleed was managed conservatively. After diagnosis confirmation, weight based anti-tubercular therapy (isoniazid/rifampicin/pyrazinamide/ethambutol) was started along with steroids at 1 mg/kg. On subsequent follow-up visits, platelet count increased and steroids were

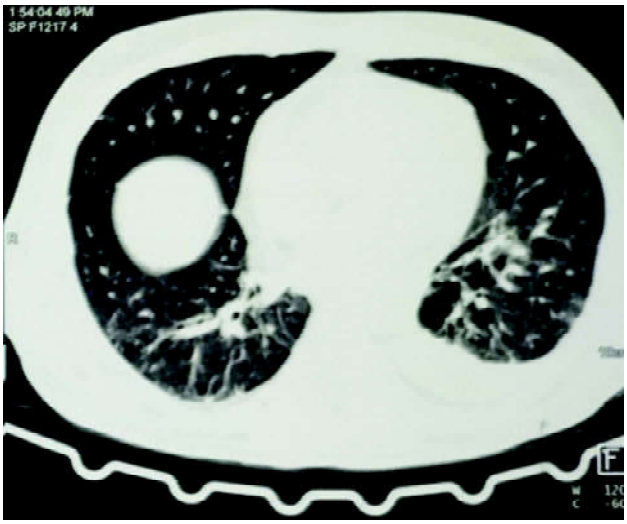

Fig. 5: *CECT Chest showing left pleural effusion.*

tapered over 6 weeks. On 10th day from discharge, the platelet count was 90,000 per cu mm and on 30th day from discharge, the platelets were 2.33 lakh per cu mm. A follow-up scan of chest and brain after 6 months showed resolution of earlier findings with normal platelet count.

Discussion

Tuberculosis-associated ITP (TB-ITP) is uncommon, with only scattered reports in the literature. The pathogenesis remains speculative but is thought to involve immune dysregulation, with the formation of anti-platelet antibodies possibly triggered by *Mycobacterium tuberculosis* antigens[1]. These immune responses may mimic idiopathic ITP but typically occur in the setting of active or latent TB infection. The clinical presentation may range from asymptomatic thrombocytopenia to bleeding manifestations; however, life-threatening bleeding, as seen in our case is very rare[2].

Diagnosing ITP secondary to TB requires careful exclusion of other causes of thrombocytopenia, including marrow infiltration, disseminated intravascular coagulation, drug-induced cytopenias, and hypersplenism. Bone marrow examination in such cases usually shows normal or increased megakaryocytes, ruling out marrow failure[3]. A key differentiating feature is the lack of sustained response to conventional ITP therapies such as corticosteroids or IVIG alone, unless ATT is co-administered[4].

The management of TB-associated ITP involves prompt initiation of ATT, which often leads to spontaneous haematologic recovery. Adjunctive corticosteroids or IVIG may be necessary in cases of severe bleeding or critically low platelet counts[5]. Our patient's platelet counts showed sustained improvement only after introduction of ATT along

with steroids, underscoring the importance of treating the underlying infection.

This case reinforces the need for clinicians to maintain a high index of suspicion for TB in endemic regions when evaluating patients with ITP. Early diagnosis and appropriate therapy can prevent serious complications and unnecessary prolonged immunosuppression.

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